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AUGUSTIN BELLOSTE AND THE TREATMENT FOR AVULSION OF THE SCALP

The Odd History of an Operation in Head Surgery

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THE perforation of the outer table of the skull in cases of avulsion of the scalp, in which periosteum is removed from the calvarium, is a procedure advised in textbooks of surgery of today, such as Homans[1] and Christopher.[2] In tracing the recorded references to the operation from these textbooks, James Robertson, through his son Dr. Felix Robertson,[3] who wrote in the *Philadelphia Medical and Physical Journal* in 1806, has been credited with originating the idea. And originator he was, so far as concerns all periodical literature since 1850, including the reports by all modern surgeons who have used the procedure and recorded their experiences with it.

A book entitled *Remarkable Cases in Surgery,* by Paul Eve,[4] and appearing in 1857, however, contains another account of the operation. It is here reprinted in full.

> Dr. Felix Robertson, the President of the Trustees of the Medical Department of the University of Nashville, was born in 1781, and was the first male child born in Nashville. In retiring from the presidency of the Tennessee Medical Society, April, 1855, he delivered an address of which the following is an extract, taken from the *Nashville Journal of Medicine and Surgery,* vol. viii, 1855.
>
> On the 11th of January 1781 he who now addresses you was born, and David Hood, in passing from the lower to the upper fort was fired on by Indians in ambush at the Sulphur Spring, in the northern part of the city. He was pierced by three balls, and fell on his face, apparently dead. The Indians rushed on him and scalped him, and stamped him on the back of the neck to dislocate it, and left him, believing he was dead. He lay perfectly still for a long time as it seemed to him, and, when he believed they had gone, he cautiously peeped about and could not see them. He then got up, and slowly wended his way toward the upper fort, a most pitiful looking object, as you may imagine; but what must have been his horror when, getting near the top of the bank, he saw the whole company on the hill but a few steps from him. He said he saw their white teeth as they laughed outright at his strange figure. He turned and tottled back as fast as his little strength enabled him, some four or five firing at him as he turned back, two balls wounding him slightly. They did not attempt to pursue him, and after passing down the ravine a little way his strength entirely failed him, he crept into the brushwood, and lay there until men went out from the forts, and found him, and conveyed him in. My father reached home late that night from a trip to Kentucky, and early next morning went in to see Hood expecting to find him, if not dead, a very forlorn case. On inquiring of David how he was, he replied "Not dead yet, and I believe I would get well if I had half a chance": my father told him he should have a whole chance and David did get well, and lived to a good old age. My father had seen many persons who were scalped in East Tennessee, and had there learned from a traveling French surgeon how to treat them. This was to perforate the outer table of the skull with a shoemaker's awl over the whole naked surface, making the perforations very close together. Through these perforations, granulations sprang up and gradually spreading, finally all united and formed a covering to the denuded skull, before it should die and exfoliate, and thus expose the brain. I am sorry that I can not recollect the name of the French surgeon who introduced the practice, for he deserves to have his name immortalized for the great boon he bestowed on the frontier settlers of that day. This operation became, in time, so common that there were persons in every fort who performed it.

While reading this amazing story of frontier hardihood, the phrase "traveling French surgeon" stimulated the present author to search further in the older medical literature, with fascinating results.

Sneve[5] in 1888 noted the above method as described in Eve's *Surgical Cases,* and used it successfully in a case of a burned scalp. In concluding his report he remarks:

> To an unknown French surgeon, therefore, belongs the credit of having conceived this most unique procedure. It would be interesting to know whether science or accident were responsible for the conception. A knowledge of the anatomy of the parts and

the physiologic laws governing the reproduction of tissues could have suggested to him the operation; and on the other hand clinical observations of granulations springing from an exposed diploë might have done so. The knowledge of this procedure seems to have been lost after a time, as there are no records that I can find of its having been resorted to on the frontier during the last 40–50 years, though numerous instances have occurred of individuals who have been thus mutilated by the Indians and recovered with bare crania.

Curiously enough, Dr. Sneve's article is the only one referring to Eve's book and the report as given in the *Nashville Journal of Medicine and Surgery* which I encountered in going through the literature. This present communication is largely an answer to all his speculations concerning the "unknown French surgeon" and his knowledge.

A search of all the literature under the subject of avulsion of the scalp, wounds of the scalp or scalping, as found in the Surgeon General's Library, the *Index Medicus* and *Quarterly Cumulative Index,* led me no nearer to the truth. Invariably the references to the origin of the procedure — and it is very pertinent to note that two German articles are included — lead to the article written by Dr. Felix Robertson[3] and published by the *Philadelphia Medical and Physical Journal* in 1806, when he was twenty-five years of age.

III. Remarks on the Management of the Scalped Head. By Mr. James Robertson of Nashville, in the State of Tennessee. Communicated to the Editor by Felix Robertson, M.D., of the same place.

In the year 1777, there was a Doctor Vance about the Long Islands of Holsten [located in the Tennessee River] who was there attending on the various garrisons, which were embodied on the then frontiers of Holsten, to guard the inhabitants against the depradations of the Cheerake-Indians. This Doctor Vance came from Augusta County in Virginia. In March of the same year, Frederick Calvit was badly wounded, and nearly the whole of his head skinned. Doctor Vance was sent for and staid several days with him. The skull bone was quite naked, and began to turn black in places, and, as Doctor Vance was about to leave Calvit, he directed me, as I was stationed in the same fort with him, to bore his skull as it got black, and he bored a few holes himself to show the manner of doing it. I have found, that a flat pointed straight awl is the best instrument to bore with, as the skull is thick and somewhat difficult to penetrate. When the awl is nearly through, the instrument should be borne more lightly upon. The time to quit boring is when a reddish fluid appears on the point of the awl. I bore at first, about one inch apart, and, as the flesh appears to rise in those holes, I bore a number more between the first. The flesh will rise considerably above the skull and sometimes raise a black scale from it, about the thickness of common writing paper. It is well to assist in getting off the scales of bone with the awl. These scales are often as large as a dollar and sometimes even twice as large.

It will take, at least two weeks from the time of boring for it to scale. When the scale is taken off at a proper time, all beneath it will appear flesh like what we call proud-flesh, and as if there was no bone under it.

The awl may, at this time, and indeed for a considerable length of time, be forced thru the flesh to the bone without the patients feeling it; but after any part has united to that portion of the scalp, which has remaining original skin, it becomes immediately sensible to the touch.

The scalped head cures very slowly, and if this kind of flesh rise, in places, higher than common, touch it with blue stone water, dress it once or twice a day putting a coat of lint over it every time you dress it, with a narrow plaister of ointment.

It skins remarkably slow, generally taking two years to cure up.

In the year 1781 David Hood was shot, at this place, with several balls, and two scalps were taken off his head, and these took off nearly all the skin which had hair on it. I attended him bored his skull and removed from almost the whole of his head, such black scales as I have described above. It was nearly three or four years before his head skinned over entirely; but he is now living and well.

In 1789, Richard Lancaster and Joel Staines were both wounded, scalped, and left for dead. These persons were under my directions; and their heads were bored as above described. They both got well in the course of 2 years.

M. Baldwin, and some others, were scalped either in the year 1790, or 1791. Their skulls I also bored or directed it to be done. They all recovered.

I never knew one that was scalped and bored as above described that did not perfectly recover. There is always part of the scalped head over which but little or no hair afterwards grows.

In 1769 I saw a young man in South Carolina, who had been scalped eight years before that time and about twice the size of a dollar of the bone of his head was then perfectly bare, dry and black. I am persuaded that had this skull even then been bored he might have recovered of the wound which put an end to his life about a year after I saw him; the naked portion of bone having rotted or mortified, and exposed the substance of his brain, a very considerable quantity of which issued out at the opening, at his death. Nashville, — April 10th, 1806.

Patrick Vance, although mentioned in this article, seems not to be remembered by modern writers. There is another record[6] of the procedure which I obtained through a descendant of Vance's.[7] From this document we learn that Patrick Vance was appointed third surgeon with the pay of assistant at Camp Lady Ambler on October 20, 1776, in the Christian campaign, which was commanded by Colonel William Christian, who was ordered to Long Island (of Holsten, Tennessee) with a force of men and reinforced by detachments under Colonels William and Love and Major Winston of North Carolina.

In Bérard and Denonvilliers's textbook of surgical technic,[8] published in 1851, there is a section on the treatment of wounds of the scalp with denudation of the cranial bone. As a first principle these writers state that if the scalp is recovered, replacement may be followed by osteo-

myelitis or early complete "agglutination." Their one case report is that of a boy who was treated by Desault by immediate replacement of the scalp. The patient recovered with but slight suppuration at the edges of the replaced scalp. The success of this case influenced their discussion of the subject, and although they discuss the opinions of La Motte, Fr. Martel, Felix Wurtz and Cesar Megatus and mention Augustin Belloste as one

LE
CHIRURGIEN
D'HÔPITAL,
ENSEIGNANT UNE MANIERE
douce & facile de guerir promptement
toutes sortes de Playes.
Avec un moyen d'éviter l'exfoliation des Os,
& une Plaque nouvellement inventée
pour le panſement des Trépans.
Par Monſieur BELLOSTE, Chirurgien
Major des Hôpitaux de l'Armée du
Roy en Italie.
A PARIS,
Chez LAURENT D'HOURY, ruë S. Jacques
devant la Fontaine S. Severin, au ſaint Eſprit.
M. DC. XCVI.
Avec Approbations & Privilege du Roy.

FIGURE 1.

Title-page of Belloste's book, 1696, containing his account of an operation for avulsion of the scalp. Author's copy.

who practiced multiple perforations, they minimize the deep concern of the older writers over the exfoliation of the denuded cranium and Belloste's method of avoiding it. This attitude was apparently that of most surgeons.

Biographically, Belloste has enjoyed the favor of the more delightful and obscure medical historians. None of the major historical writers have mentioned him in the role of contributor to medical progress. An almost contemporary account of his life was recorded in 1778 by Eloy.[9] A translation from the French follows:

> Belloste, Augustin, was a great surgeon of Paris where he was born in 1654. He served with distinction in the armies and hospitals of the Most Christian King of France; but the Duke Victor Armedee of Savoy, King of Sardinia, removed him to his kingdom in 1697 and placed him at the service of the Queen, his mother, in the rank of first surgeon. In 1695 he first published a book entitled *Surgeon of the Hospital, and a Method to Heal Wounds Promptly,* of which there are many different editions. We note those of Paris in 1696 [Fig. 1], 1698, 1705 and 1715, in octavo; of Amsterdam in 1707, in octavo; of Dresden in 1703, 1710 and 1724, in octavo, translated into German by Martin Shurig. In 1725 Belloste published *Sequel to the Surgeon of the Hospital,* which appeared the same year in Paris, and again in 1728 in duodecimo editions. In this he combined his important observations on the effects of mercury and the use of this mineral with purgatives. His treatise on mercury was reprinted in 1738 in duodecimo. Denis Sancassani put the whole work into Italian under the title of *The Surgeon in the Field* (Venice 1729), two volumes, in octavo; one may say that it has been translated into almost all the languages of Europe. So many editions and versions amply prove the high estimation in which this book was held. Belloste took from the ancients methods which had been neglected and thereby made a name for himself which is still upheld. It is following Celsus that he advises piercing the carious bone with the point of a trephin to accelerate exfoliation; and from Cesar Magatus that he demonstrated the danger of tampons and frequent dressings in the healing of wounds.
>
> There are some letters of this surgeon in the works of Sancassani, who speaks of him with great respect. He was also respected by the public for his success in the practice of his art, and he still enjoyed a brilliant reputation when he died at Turin on July 15, 1730.

Belloste[10] in 1696 wrote as follows:

> If the bone is uncovered for a considerable extent, with loss of substance, the wound cannot heal for a long time because of its size, and one is not able to prevent the bone from becoming altered and carious, by whatever precautions that might be taken. Now in order to avoid this accident it is necessary at the first dressing, or as soon as possible, to pierce the bone in several places with the pyramid or perforator of the trephin; in this manner one gives passage to a marrow juice which, oozing out, covers the bone in a short time without loss of the least part of its substance.
>
> To be a surgeon, one should know that whenever the bone is uncovered for a considerable area, it is impossible for the soft parts to regenerate without recourse to the Art [of surgery], because the surface is very smooth and polished. It is this fact which obliged most of the ancients to apply the rasp to make it rough and at the same time to open the orifices of the small vessels, of which the internal substance is filled, in order to furnish the blood which is necessary to produce new flesh which heals it.
>
> But the operation which I have done on several occasions and which I propose here seems to me more prompt, sure and useful than the rasp, which while passing several times over the surface of the uncovered

bone, heats and alters it much more than the perforator which touches but lightly, at slight intervals from each other, and which penetrates far enough to reach the diploë from which one draws the help we need. Moreover, the rasp diminishes the thickness of the bone, and subjects the patient to pain, which one avoids by this operation. . .

The bone of the cranium takes its nourishment from three separate sources, according to the opinion of several authorities. Firstly, from its under surface or internal portion, which is next the brain, through the vessels of the dura mater. Secondly, from the central part which is between the tables; it is nourished by a marrow juice which, arising from the diploë, communicates to the two tables and furnishes them the necessary food. Thirdly, on its external aspect it is nourished and protected by the periosteum by which it is covered for its entire extent.

Thus when by some outside violence the bone is scalped of this, so that it remains uncovered, it is well assured that the air attaches itself to the external surface with its acid and nitrous points, which in a short time alter and decay it; it is necessary then that it exfoliate because it is deprived of nourishment and the air finds it without defense.

It is then necessary to find a means of repairing the loss to the bone and to find in the neighboring parts food which takes the place of that lost, and which at the same time in covering it shelters it from external injuries. Such cannot be found closer than in the diploë, but to have it, a passage must be made and open to it easy pathways to fulfill at the same time the intention of Nature and that of the surgeon. When the bone is opened as described above, the diploë pushes through these little passages the most subtile parts of its marrow juice, which, coagulating in the bone in three or four or five days, sometimes more or less, completely cover it. . . .

One will have a little hesitation in using this technic if one realizes that it avoids about forty days before exfoliation and the time thereafter necessary to granulate and cicatricize the ulcer, all told taking the poor patient almost sixty days in place of twelve or fifteen at the most following this method.

Belloste then records the cases of two soldiers with moderate-sized wounds which required eighteen and seventeen days respectively for healing.

There are a number of interesting sidelights which turned up in the older literature. Jacobus Renatus Tenon,[11] for whom Tenon's capsule of the eye is named, took a very active interest in Belloste's idea, indeed so much so that he used a number of dogs as subjects of observation in controlled experiments. He denuded both sides of the skull and perforated the outer table on one side with a trephine about the size of a "12 sous piece." Various dressings then in vogue were applied to both sides, such as, water, wine, balsam of Peru, basilicum, *platre de mastique, l'eau mercuriale,* and in some animals the skull was exposed to the air. His final conclusion was that perforation did not aid healing of the wound enough to justify its use. However, the size of his opening, which caused excessive formation of granulation tissue, was larger than either Vance or Belloste advised. Let us observe that the publication of these results was in the year 1806, the same as that in which Robertson's[3] account was published in Barton's journal.

The writers of the older books of surgery (Hippocrates,[12] Galen,[12] Celsus[13] and Fabrice d' Aquapendente[14]) knew that baring the calvarium of periosteum was a severe wound and that the outer table often became carious, finally either exfoliating or causing an osteomyelitis, sometimes fatal. Celsus advised the perforation of the dry, blackened sequestrum with an awl or terebra some time after the injury. Fabrice, following Galen's practice, recommended rasping the denuded cranium. All these writers deferred action until delineation between sequestrum and normal bone had occurred. One curious and questionable case, reported by de Marchettis,[15] and antedating Belloste, was that of a seven-year-old boy from the orphanage at Batavia who had his scalp torn off by a bear. Granulations arose from between the sutures and covered the head in fifteen days, and in three months the entire wound was healed and hairs were even growing in the scar.

The problem then resolved itself into the necessity of explaining why the only link between modern literature and the old textbooks should be through but one man: Patrick Vance. None of the nineteenth-century English or American texts on surgery contain any reference to the procedure. Perhaps the authors knew of it but regarded it as of no account.

From a descendant of Dr. Vance,[7] it was learned that his full given name was Kilpatrick. He was born in Scotland and claimed to be a graduate of the University of Edinburgh. It is not known when he came to this country. A letter[16] from the dean of the School of Medicine of the Royal Colleges, Edinburgh, who made inquiries in the Library of the College of Physicians there, states: "There is no evidence that he ever took the qualification here, and his name does not appear on the list of graduates in Edinburgh, Glasgow or Aberdeen." However, Comrie's *History of Scottish Medicine*[17] states that most of the men who founded the Royal College of Physicians and the Faculty of Medicine at Edinburgh were graduates of French universities or had studied under Boerhaave at Leyden, and that Boerhaave's books were used extensively as texts for the students at the time when Kilpatrick Vance was presumably studying there.

Comrie further states:

During the latter half of the eighteenth century Edinburgh was the great medical resort of all Britons beyond the seas, much as Leyden had been the resource

for those who wished to take a medical degree half a century earlier. The number of graduates is not however an indication of the number of students, for, while many men who studied medicine at Edinburgh took the qualification of the College of Surgeons, right up to the passing of the Medical Act in 1858, a large number of students were content to learn their profession as apprentices to some practitioner and to take a few classes at some medical school such as Edinburgh without proceeding to qualification.

In Boerhaave's *Aphorisms*[18] we find:

> *249.* If the Pericranium, or Hair Scalp be so much wounded that it discovers the Bone for a long while or that it putrefy, the Bone is deprived of the Vessels of the Periosteum and consequently of its own; the Liquor is then stagnate, and, being putrefied, separateth a Scale; after which, the Bone, grown yellow, dusky and black, doth deposit a Leaf. . . . *252.* The Cure is effected: 1. By piercing the Bone as deep as its Middle with a little Trephan, applied to several but near adjoining Places, whereby Exfoliation is prevented and the Periosteum is made to grow again. . . . *253.* By which Method there ariseth out of all these Perforations and from all Sides in a small Time, as it were, a new fleshy Substance and afterwards the Rest heals.

Van Swieten[12] in his commentaries on the aphorisms of Boerhaave gives Belloste full recognition for stating the above; especially does he emphasize that it is a primary and not a secondary procedure. He also records Belloste's two case reports.

Belloste's significant contribution was to state that small perforations of the outer table should be made at the primary dressing of the wound, thus entirely avoiding exfoliation or sequestration. The method has been used by modern authors.

Here, then, is the story of a definite surgical procedure which, so far as can be found, originated with one man, Augustin Belloste, in 1696; passed from Boerhaave to Patrick Vance; and carried into modern literature through the medium of two Americans — Felix and James Robertson. No other authors have ever claimed to have thought of the method independently. This is a very peculiar sequence of events, which has combined to preserve for us one small bit of surgical lore. Others even more valuable must have been lost. Such are the vagaries of history.

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CHEMICAL STRUCTURE: BIOLOGICAL ACTION: THERAPEUTIC EFFECT*

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BOSTON

THE discussion of the inter-relation between chemical structure, biological action and therapeutic effect seems to be timely. Research activities in fundamental and applied sciences continue to increase. The question is being raised whether universities should take part in these varied activities or restrict their interests to the cultivation of selected disciplines. As a further complication, an increasing number of research institutes have been established in recent years by foundations and by industrial corporations. What is to be the future role of these institutions? Should the less well-equipped university departments, in order to avoid duplication, intentionally cultivate a more fundamental type of investigation and more general correlations? Should there be any sort of inter-relation between university departments and these research institutes? Should industrial research laboratories be used for the temporary training of a limited number of mature students in science, in the same manner as the clinic is used for medical students? Whatever the final answer, we must be cognizant of these changing activities, which are of potential significance.

The question has also been raised by those who are interested in these problems and who are trained primarily in chemistry, as to whether the biological sciences and clinical medicine, in particular, are not unduly lagging behind chemistry. One branch of the biological sciences, namely pharmacology, has been particularly criticized. The correct appraisal of this question is a primary concern of those associated with a medical school.

I shall confine this discussion to an analysis of one phase of this topic.

By citing a few selected examples, I propose to supply an explanation for the following conclusions: (1) Notwithstanding skepticism, important progress has been made in recent years in the field of knowledge which depends on the proper integration of chemistry, certain medical sciences and therapeutics. (2) While from a theoretical point of view there exists an ideal method of correlation of activities between these fields, in practice important advances and discoveries often fail to follow such a set pattern. (3) As most human ailments cannot be reproduced in animals, and as disease often represents not only quantitative but also qualitative change in functions and structures, study of the action of chemical substances in human disease remains an essential discipline. If today this field is not cultivated in the right way, it does not mean that the subject cannot be made a branch of science. (4) There are good reasons why progress in the chemical aspects of the biological sciences, particularly pharmacology and therapeutics, will always lag, at least apparently, behind chemistry. (5) While this field of activity is cultivated by all branches of chemistry and medical sciences, proper emphasis on and better correlation of the subject in the future may lead to progress of both theoretical and practical significance. Let us now examine these points in greater detail.

The reason for the apparent lag of the chemical aspects of biology and medicine is clearer today than it was formerly. Organic chemistry and biochemistry are relatively young. Pharmacy and therapeutics, on the other hand, are considerably older. Many significant discoveries in therapeutics were made, on purely empirical basis, many years or even centuries ago. The use of opium for the relief of pain and diarrhea, of cinchona bark in malaria, of coca leaves for relief of fatigue, of cod-liver oil and certain fruits in nutritional deficiencies, of iron in anemia, of digitalis in heart failure and of ephedra twigs as a stimulant are examples of such early therapeutic discoveries.

With the development of organic chemistry, toward the end of the nineteenth century, there were those who expected that the application of this new field to medicine not only would at once open up new avenues in pharmacy but would rapidly lead to discoveries of new cures for disease. Some of the therapeutic discoveries and the rapid initial development of experimental pharmacology at the beginning of the present century seemed to confirm and enhance such an optimistic expectation. Certain results during the past two decades, on the other hand, have injected skepticism into the rapid triumph of organic chemistry in medicine.

The chemist, who continues to prepare sub-

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stances with dispatch, clamors impatiently for an answer from the worker in biological sciences as to the value and significance of his compounds. Before the final answer as to the therapeutic efficacy of a chemical substance can be given, however, numerous questions have to be answered, and the answer to each requires repeated and tedious investigation. To ascertain the relative efficacy, toxicity and persistence of action under various routes of administration is merely a beginning. Long-continued experiments must follow the short ones. The biological characteristics of the compound should be ascertained in many species of animals and often in lower organisms. There follows a search to determine the physiological and pharmacological effect on various tissues, organs and systems. Eventually as many of these features as is feasible have to be investigated in normal man. Finally, it is necessary to study the effects and biological characteristics of the compound in different diseases. Because the experimental therapeutic approach in diseased persons is limited, it is also essential to study the effect of an agent in disease induced in animals. After encouraging preliminary investigations, a drug may fail to be useful simply because one of its many biological characteristics is not in accord with the therapeutic problems of the specific disease for which it was intended. A vasodilator substance, for example, may fail to be useful in a certain disease simply because it has to be given intravenously or because it has only a short persistence of action. Obviously, with all the investigative opportunities available, it is feasible to supply answers to all these questions for but a limited number of substances. Hence, whereas the chemist can prepare a substance rapidly, medicine must give the answer slowly. It is sometimes discouraging to find that long years of worldwide clinical application of a chemical substance are necessary before its serious untoward reactions are discovered. I refer to such examples as amidopyrine, causing agranulocytosis; cinchophen, producing acute yellow atrophy of the liver; codeine, responsible for drug addiction; arsphenamine causing blood dyscrasias; and phenobarbital (Luminal) or allyl-isopropyl-acetyl-carbamide (Sedormid), causing serious skin rashes.

If a chemical substance reveals a certain biological action which makes it a possible but not an ideal therapeutic agent, attempts are often made to alter the chemical structure with an expectation, rational from a biochemical viewpoint, of obtaining the desired action. Not infrequently, however, the answer supplied by the experimental and clinical studies is different from the theoretical expectation. Such experiences further strengthen the need for prolonged investigation.

A few specific examples bearing on such recent activities in this field will make these points clearer. Let us consider, therefore, three groups of substances as illustrations: barbiturates, sympathomimetic drugs and the morphine group.

BARBITURATES

Thirty-five years ago Emil Fischer and von Mehring established the fact that while barbituric acid, a derivative of urea and malonic acid, is physiologically relatively inactive, the substance obtained by replacement of the two hydrogen atoms by ethyl radicals is a powerful hypnotic in animals and man (Fig. 1). Since this discovery a

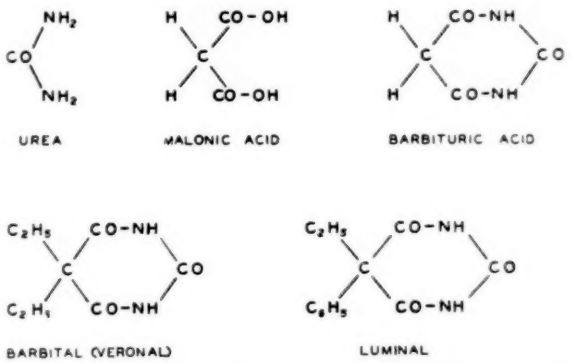

FIGURE 1. *The Chemical Structures of Urea, Malonic Acid and Barbituric Acid, Which Possess No Hypnotic Effect, and of Their Ethyl and Phenyl Derivatives, Veronal and Luminal.*

large number of other barbituric acid derivatives have been prepared by replacing one or both hydrogen atoms by alkyl, cyclic and other radicals. Partly through their beneficial effect in certain conditions and partly through the zeal of manufacturing houses, these substances have become widely used in different branches of medicine. The barbituric acid derivatives are certainly among the most widely used drugs today. Veronal, Luminal, Ipral, Amytal, Allonal, Dial, Pernocton, Somnifen, Nembutal and Evipal are but a few of the trade names of the more commonly used barbituric acid derivatives.

A number of significant facts have been brought to light as a result of these studies. It has been found that often the hypnotic value and the toxicity of members of the group have been increased by substitution of the two hydrogen atoms by longer and more complex alkyl or cyclic radicals. The anesthetic value was found to be relatively higher in the ethyl-iso-butyl, the ethyl normal butyl, the ethyl-iso-amyl and the ethyl normal hexyl barbituric acids.[1] Investigation revealed also remarkable differences in the excretion of the

various derivatives. Thus from 60 to 90 per cent of diethylbarbituric acid (Veronal) is eliminated through the kidneys, while other barbiturates are almost completely destroyed within the body. Marked differences have also been found in the persistence of action of the various members. Barbital (diethylbarbituric acid) and Luminal (phenobarbital) have a persistence of action of many hours' duration, while the effect of Evipal (cyclo-hexamyl-methyl-n-methyl barbituric acid) lasts but a few minutes after intravenous administration. In the latter substance we possess a hypnotic with a complex side radical. This side chain is instantly metabolized in the body, and thus a biologically active compound is changed into one which is inert. The time element of induction of sleep also varies considerably. The sleep induced by some barbiturates is preceded by excitement, while others do not produce this effect.

If we wish to use a sedative as a preventive of convulsions in epilepsy, we use a barbiturate with long persistence of action, such as phenobarbital, in small doses. If we wish to combat severe convulsions we use the same type of barbiturate in large amounts. If we wish to induce natural sleep we select members with shorter persistence of action, in order to avoid a hang-over the next day. Pentobarbital sodium (Nembutal) and iso-amyl-ethyl barbituric acid (Amytal) are such barbiturates. If prompt anesthesia and relaxation of the muscles are desired, as in the treatment of fractures or dislocations, we administer Evipal intravenously and obtain the desired result for but a few minutes.

Studies of the barbiturates, particularly during the last ten years, have enriched medicine by providing a group of useful drugs which are administered in the treatment of insomnia, poisoning from local anesthetics, epilepsy, pain in childbirth and eclampsia. These drugs are also useful for the better induction of general surgical anesthesia. Today we have also adequate knowledge of the danger involved when barbiturates are used in large amounts, or when they are administered to persons with an idiosyncrasy to certain members of the group. We know that certain barbiturates are responsible for skin diseases and blood dyscrasias. In case of barbiturate poisoning, effective antidotes have been found in drugs such as picrotoxin, ephedrine and strychnine. Thus after making due allowance for unsupported claims, the accomplishments make the investigations of the past more than justified.

SYMPATHOMIMETIC DRUGS

It is fitting to discuss here the sympathomimetic group of drugs, not only because of their widespread therapeutic use, but also because this group is of considerable significance to chemists, physiologists and pharmacologists in developing an understanding of the relation between chemical constitution and biological action.

Achievements in this field are the result of varied and quite independent investigations. Our knowledge is based on the discovery of a vasopressor effect of extract of the adrenal by Oliver and Schäfer and by Czybulsky and Symonovicz in 1895. Takamina's discovery of crystalline epinephrine in 1901 stimulated interest in the chemistry of this substance. Barger and Dale's classical study in 1910 on the relation between the chemical structure of aliphatic and aromatic amines and their sympathomimetic activities established important chemopharmacological principles. More recently, efforts to identify chemically the "adrenergic" mediators of nerve impulses have injected a new stimulus into this field, mainly as a result of the work of Cannon, Loewy, Bacq and Rosenblueth.

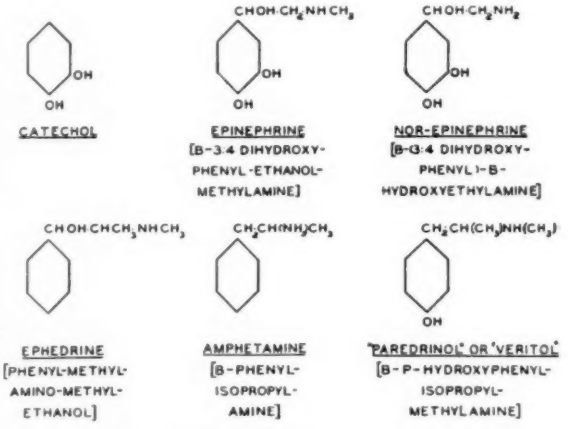

FIGURE 2. *The Chemical Structures of Some of the Sympathetic Amines with Biological and Therapeutic Actions.*

Meanwhile, quite independently, Chen and others[2, 3] have studied a number of alkaloids isolated from the ancient Chinese remedy ma huang. These alkaloids also turned out to be sympathomimetic aromatic amines, related in their chemical structure and pharmacological action to ephedrine. Finally, attempts have been made by chemists to prepare new compounds, with the expectation of obtaining agents with more desirable action.

These groups of sympathomimetic amines have as their prototype l-epinephrine, which consists of a catechol nucleus to which aliphatic side chains are attached, in which alcoholic and amine groups are substituted (Fig. 2). The number of known related amines is great, and possible chemical variants are unlimited. These different amines exert different biological actions, some of which bear

in an important way on therapeutic applications. Already Barger and Dale have noted differences in pressor effects of various members in the capacity of ergotoxin to inhibit the vasopressor effects and in causing relaxation of the isolated, nonpregnant uterus of the cat.

The sensitivity of biological responses to slight chemical changes is strikingly illustrated by the difference in the potency between levo- and dextro-epinephrine. Pressor responses to a given dose of l-epinephrine are much greater than those induced by the corresponding d-isomer. The duration of the response is more prolonged, on the other hand, in the case of the d-isomer. It may be pointed out here that the ratio of the muscular contracting power to the relaxing power of the d- and l-epinephrines is not definitely known, in spite of the fact that epinephrine has been investigated extensively. This illustrates the fact that certain pertinent and obtainable knowledge is still lacking, even in such an extensively studied and important substance.

Chen has pointed out that the phenolic groups in the epinephrine molecule are responsible for the intensity of action. With the entrance of a methyl group in the α carbon atom, ephedrine appears to acquire increased duration of action. Chen found that the primary amines are more active than the corresponding methylated secondary or tertiary amines, especially with reference to pressor action (Chen, Wu and Henriksen[3]).

Figure 2 demonstrates the chemical structure of a few of the sympathomimetic substances. While all these compounds possess vasopressor effects, they differ in several important ways. Catechol, for example, in contrast to other sympathomimetic drugs, exerts a convulsant and cardiac depressor action (Tainter[4]). Epinephrine and nor-epinephrine differ mainly in that ergotoxin reverses the pressor response to epinephrine, but not that of nor-epinephrine. Nor-epinephrine has a greater intrinsic power of inducing contraction of certain smooth muscle cells than has epinephrine. Epinephrine, on the other hand, has a much greater intrinsic power of inducing relaxation. Nor-epinephrine is suspected by some (Greer, Pinkston, Baxter and Brannon[5]) to be one of the adrenergic mediators of sympathetic nerve impulses, corresponding to sympathin E of Cannon and Rosenblueth.[6]

The differences in effect of epinephrine and ephedrine consist mainly in the effectiveness of ephedrine after oral administration, in contrast to that of epinephrine. The vasopressor and cardiac stimulant effects of ephedrine are much less intense but more prolonged. Ephedrine is a less efficacious bronchorelaxor agent, but it possesses a remarkable stimulating effect on certain brain centers, which makes its action, in contrast to that of epinephrine, quite specific in certain conditions associated with sleep or coma, including narcolepsy.

The two synthetic compounds of amphetamine (Benzedrine) and paredrinol (Veritol) possess interesting pharmacological and therapeutic qualities. In its structure and action amphetamine is closer to ephedrine, while paredrinol resembles epinephrine. Amphetamine exerts less vasopressor, cardiac and bronchial effect, but has a greater central effect than does ephedrine. It has a remarkable action in decreasing or abolishing the sensation of fatigue. Its central stimulating effect makes it particularly suitable in the treatment of narcolepsy and in certain types of paralysis agitans.

Paredrinol is a compound with mainly vascular effect and without significant central nervous action. In contrast to amphetamine it is ineffective in narcolepsy. In contrast to epinephrine, it produces prolonged vasoconstriction after oral administration. The vasoconstriction involves both the arterioles and venules, but arteriolar constriction is not out of proportion to the elevation of the blood pressure. Tissue ischemia, observed after epinephrine, does not occur as a rule after the administration of paredrinol. From both experimental and clinical considerations, paredrinol seems to be a suitable therapeutic agent, while epinephrine is not applicable in certain types of collapse and shock.

MORPHINE GROUP

Advances in knowledge in this group of alkaloids are also instructive in the light of what has been said in the introduction to this discussion. Morphine is one of the most useful drugs. In China the use of opium dates back as far as the recognition of cholera there. The stalk of the poppy plant is mentioned as an ingredient of an Egyptian prescription in the *Papyrus Ebers*. The juice of the poppy was certainly an effective remedy in the hands of physicians of ancient Greece. Pliny was probably the first to use the word "opium." During the centuries immediately following, some progress was made in the effective use of opium preparations. The first milestone in this field, however, came with the contributions of the young German pharmaceutical apprentice Sertürner, who in a series of reports published between 1805 and 1817 described the isolation and certain pharmacological characteristics of morphine. Thereafter, as a result of the development of organic chemistry, experimental pharmacology and clinical medicine, valuable information was acquired concerning the chemistry and the biological action of morphine and certain related compounds.

In recent years, after a period of relative stagnation, interest in the field has been renewed. The new tools applied were those of synthetic organic chemistry. These recent efforts consist mainly in the preparation of new compounds through alteration of the morphine and codeine molecules, with the primary purpose of obtaining drugs with some of the therapeutic effects of morphine but without its undesirable effects (Fig. 3).

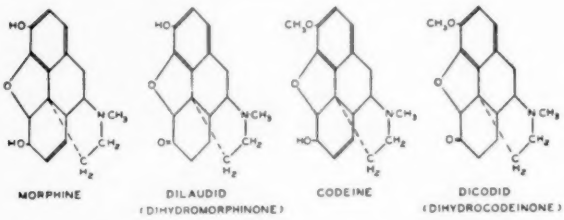

FIGURE 3. *The Chemical Structures of Morphine and of Related Compounds.*

Codeine, which is chemically but a slightly altered morphine derivative, a methyl morphine, is about twenty times less toxic than morphine. It is only fairly effective as a therapeutic agent in the control of cough, and but slightly effective in the relief of pain. Up to the present codeine has not been regarded as a drug producing addiction. The story of its discovery as a drug of addiction is mentioned here to demonstrate how long a clinical fact may escape recognition. In 1927 the discovery was made in England that the importation of codeine had increased remarkably and that the drug had to some extent replaced morphine among addicts. In 1931, however, a group of experts appointed by the League of Nations expressed the opinion that codeine was harmless and did not produce addiction. Evidence that the drug was used extensively by addicts nevertheless continued to accumulate. Smuggling of the alkaloid into Canada had become disquieting, and illicit entry across the border into the United States had grown alarmingly. One of the experts mentioned reinvestigated the entire problem, and has called attention to the codeine danger.[7] He refers to experiments performed on animals with habit-forming drugs as more or less valueless. He also points out that there is little or no analogy between monkeys and human beings in their reactions to codeine, while in rabbits and other mammals the alkaloids of opium are apt to give rise to tetanic convulsions.

The biological properties, including the analgesic and respiratory action, of Dilaudid (dihydromorphinon hydrochloride) are quite similar to those of morphine, but Dilaudid is more than twice as toxic, as well as twice as effective. While tolerance to this drug develops less easily than does that to morphine, addiction has been reported. Dilaudid has a certain limited therapeutic use in preference to morphine.

The pharmacological and therapeutic properties of Dicodid (dihydrocodeinon bitartrate) are closer to those of morphine than to those of codeine. Its respiratory-depressant and sedative effects are claimed to be more marked than those of morphine. Its narcotic and analgesic effects are less. Dicodid, in contrast to morphine, does not cause constipation. The tendency to addiction after its prolonged use is less than after morphine.

Numerous additional efforts have been made in recent years to find useful therapeutic agents through changes in the morphine molecule. The practical applicability of the results of these studies cannot as yet be evaluated. In spite of the numerous new compounds which have been prepared and tested, it may be stated that so far no substance in this group with effective sedative or analgesic qualities is known which is not, at least to some degree, associated with a tendency to habit formation and to addiction.

OTHER EXAMPLES

This discussion could be widened by presenting numerous additional examples of chemicopharmacological correlations. The choline derivatives are of special interest today, as they play a fundamental role in physiology, pharmacology and therapeutics. Studies of the sulfanilamide group have resulted in therapeutic triumphs in certain infectious diseases. Systematic investigations of carbon tetrachloride, tetrachlorethylene and hexylresorcinol groups have made possible more effective treatment of parasitic intestinal infestations. Finally, recent discoveries and correlations of the chemistry and biological action of substances related to phenanthren, cholesterol, vitamin D, estrogenic substances and the digitalis glucosides are opening up possibilities for a better understanding and the establishment of an inter-relation between the fundamental problems in the etiology of cancer, in the development of arteriosclerosis, in sex function and in myocardial failure. Perhaps with the development of this new knowledge the most instructive lessons can be drawn from the relation between molecular arrangement, function and cellular structure. This fascinating new chapter in medicine has been admirably summarized by Butenandt.[8]

In several important therapeutic advances the initial discovery and stimulus were provided by observations of the clinician at the bedside. The classic discovery of the efficacy of liver in pernicious anemia has stimulated important chemical investigations. The observation of the beneficial effect of Prostigmin (previously used only for the

treatment of abdominal distention) in patients with myasthenia gravis has yielded new insight into muscular physiology and pathology. Similarly, the empirical discovery of the therapeutic value of quinine in myotonia congenita has stimulated physiological studies on the striated muscles.[9] The casual clinical observation that a high-fat diet, devised for the treatment of epileptic children, has resulted in a rapid clearing up of co-existent pyelonephritis instigated a systematic investigation of the bactericidal effects of various organic acids. These studies in turn led to the important discovery of the value of mandelic acid in the treatment of certain types of pyelonephritis.

* * *

Here, then, is a field of great significance for the future development of medicine. It should be cultivated in the future not less but more than in the past. If physicians are to maintain an interest not only in analytical but also in synthetic activities, they must foster more intensely this triple interest of correlations. Such increased knowledge will give better insight into the secrets of life, and at the same time will assure better care of the sick. Therapeutic skill must depend not on an innate, intangible gift, but rather on a rational analysis and definition of the patient as a psychophysical unit, and on a knowledge of the possibilities as well as the limitations of those physical, chemical and abstract measures which improve or re-establish health.

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THE TREATMENT OF TETANY WITH DIHYDROTACHYSTEROL (A.T. 10)*

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IN 1936, when dihydrotachysterol first became available in this country, we were fortunate in obtaining a supply for trial in the treatment of parathyroid tetany.* It at once became obvious that it caused an elevation of blood calcium toward normal and adequately controlled the symptoms of tetany. Being effective by oral administration, it promised to be the most convenient and effective method of controlling severe tetany. We immediately encountered two difficulties. In the first place, the cost of the material made its use undesirable by some patients with mild tetany which could easily be controlled by the oral administration of calcium lactate. Secondly, our doubts as to its value in all cases of severe tetany were raised by an apparent failure to elevate the blood calcium and control symptoms in a very severe case (Case 1); it was later learned that the apparent failure was due to lack of co-operation by the patient.

Dihydrotachysterol is known as A.T. 10 (antitetanic preparation Number 10), a derivative of irradiated ergosterin, and is said not to be antirachitic. Introduced first by Holtz,[1] there have been numerous articles on its clinical use since then. Albright and others,[2] through their studies on its effect on calcium-phosphate metabolism, have concluded that A.T. 10 is the most efficacious therapeutic agent in the treatment of tetany. The reader is referred to their review of the literature for a fuller bibliography.

Vitamin D acts like A.T. 10 in facilitating calcium absorption from the intestinal tract, but its action is slower and there is less excretion of phosphorus in the urine. Both drugs raise the level of the blood calcium. Parathormone, while raising the blood calcium, is thought by Albright et al.[3] not to have any action on calcium absorption from the intestinal tract, although there is marked phosphorus secretion in the urine. This observation, in addition to the necessity of hypodermic injection, makes parathormone give way to the oral use of A.T. 10 in the treatment of tetany.

We have used A.T. 10 in 6 cases of postoperative tetany. All these patients had had tetany for two years or more, so that their status was

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well known, and with 2 exceptions were symptomatically controlled with calcium by mouth. Of this group, only 3 patients are still taking A.T. 10, the remainder having had to discontinue its use because of its high cost. It is hoped that this obstacle will soon be overcome so that it may be available to patients with average incomes.

In several of the milder cases, all calcium by mouth was stopped for from two to four weeks; A.T. 10 was then begun in doses ranging from 12 to 20 cc. during the first four or five days, but thereafter reduced to 1 cc. daily or 1 cc. every other day. In severe cases calcium was stopped and A.T. 10 was begun immediately in larger doses, but shortly thereafter 1 to 3 cc. daily was prescribed. Later, available calcium in the form of calcium lactate, chloride or gluconate was prescribed orally.

No toxic symptoms were observed except in those cases in which the blood calcium rose above normal. Two patients (Cases 2 and 3) had a hypercalcemia. One of these (Case 2) developed headache and the patient had an extreme aversion to taking the calcium; nausea was also present. The other patient (Case 3) complained of loss of appetite, nausea, headache and lassitude. Both patients soon lost their symptoms when A.T. 10 was discontinued; one (Case 3) even went through pregnancy without additional medication. Following delivery the dose was increased, during which time hypercalcemia developed.

The daily requirement of A.T. 10 apparently depends on the extent of the deficiency. Doses of 2 to 5 cc. weekly are sufficient to control the milder moderate cases, while severe cases may require larger doses. Large doses are taken during the first week of treatment; the level of blood calcium is determined at least weekly thereafter. When the blood calcium has reached a normal level, an arbitrary dose of 0.5 to 2.0 cc. is prescribed until the daily or weekly requirement is worked out. It is advisable to give calcium by mouth whenever it can be tolerated, as it reduces the amount of A.T. 10 required and in turn provides soluble calcium. In spite of arguments in favor of other calcium preparations, calcium lactate in our experience has been the best-tolerated form. Blood phosphorus levels have varied. In some cases, particularly when hypercalcemia was present, there was a marked drop; then the blood phosphorus rose again and the calcium dropped. In general, the average blood phosphorus level was lower after treatment. In one patient (Case 4), in whom severe hypertension developed, there was a gradual rise in the phosphorus level although the use of A.T. 10 was intermittent. In this case its employment in this manner required less calcium, and there were longer periods of freedom from tetany.

CASE REPORTS

Case 1. A 20-year-old woman entered the clinic December 1, 1936, complaining of "spells" which had occurred during the previous 10 months after subtotal thyroidectomy had been performed at another institution. These spells were typical of severe tetany and often ended in unconsciousness.

Examination showed that the patient was well developed and nourished. Marked exophthalmos was present, the pulse was 100 and no thyroid remnants could be palpated. The blood pressure was 140/80. The heart and lungs were normal. Chvostek's and Trousseau's signs were easily elicited. The patient entered the hospital 2 days later, at which time the level of the blood calcium was 6.7 mg. per 100 cc., and that of the phosphorus 7.9 mg.; two days later the value for calcium was 6.7 mg., and for phosphorus, 8.6 mg. The patient was given calcium lactate with some improvement and was then started on A.T. 10 (Fig. 1) but this was discontinued because she said it caused diarrhea. Some months later the patient revealed that she had been taking a large dose of mineral oil which had been secretly given her at the hospital, and which undoubtedly accounted for the looseness of the bowels.

The patient was then given large doses of calcium and vitamin D concentrate. The blood calcium reading in January, 1937, was 8.1 mg. per 100 cc., and that of phosphorus 7.1 mg. Doses of parathormone were gradually increased, and she returned to the clinic with acute tetanic seizures, quickly relieved by intravenous injections of a 10 per cent solution of calcium gluconate. During this time she was given a diet low in milk, meat and eggs, without appreciable effect. In March she was taking 500 units of parathormone a day and said she took from "½ to 1 lb." of calcium lactate daily. The value for the blood calcium at this time was 8.1 mg. per 100 cc., and she was getting along fairly well. On March 29 the blood calcium reading was 9.3 mg. per 100 cc., and that of the phosphorus 5.9 mg. The patient continued on this regime, and in May entered the clinic with another attack of acute tetany. She had had several of these attacks while in neighboring cities. At this time she was taking 50,000 units of vitamin D, 300 to 400 units of parathormone and 10 teaspoonfuls of calcium lactate in powder form and ten 10-gr. tablets of calcium lactate daily. Calcium chloride was again advised, but she could not tolerate it. From May 27 to July 1 the tetany was never adequately controlled and she had frequent attacks. All during this time Trousseau's and Chvostek's signs were positive. A.T. 10 in larger doses was begun, in addition to parathormone and large quantities of calcium. A blank space has been left in the chart for an interval during which the amounts of parathormone and calcium that were ingested are unknown; on one occasion during this period she was ordered to take 20 to 30 cc. of A.T. 10 daily for a few days. On July 14 the blood calcium was 8.9 mg. and the phosphorus 7.1 mg. per 100 cc., and Chvostek's sign was positive. On July 23 she was advised to take 15 cc. of A.T. 10 daily. On August 4 the level of the blood calcium was 9.9 mg. and that of the phosphorus 4.1 mg. per 100 cc., Chvostek's sign was negative and she was feeling well, being free from tetany. She was advised to reduce the dose to 7 cc. a day; the case was followed until September, the dose being cut down gradually to 4 cc. and 1 teaspoonful of calcium chloride four to six times a day. The value

for the blood calcium remained normal, Chvostek's sign was negative, and dosage was further reduced to 1 cc. and then to 0.5 cc. daily. The blood calcium gradually fell to approximately 7 mg. per 100 cc., and the patient was advised to increase the dose to 1 cc. daily for an indefinite period.

The patient was not seen again for some months. When seen in April, 1938, she said she had not taken A.T. 10 normal, and following this she obeyed instructions explicitly. She has also assured us that she took the prescribed quantities of calcium and parathormone.

Case 2. The patient, a 28-year-old unmarried woman, was first operated on in the clinic in 1918 for exophthalmic goiter. In 1921 there was a recurrence of hyperthyroid symptoms. Lugol's solution was given but failed to control the symptoms, and in 1931 she was operated on be-

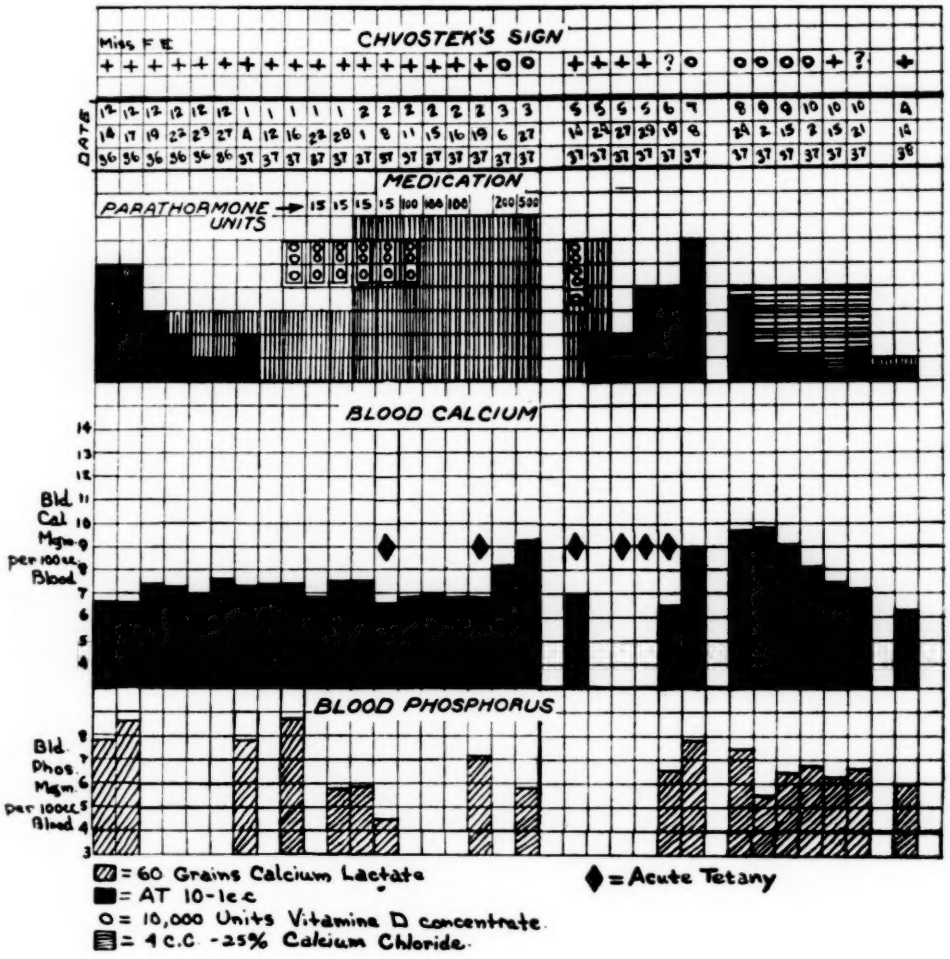

FIGURE 1. *Case 1.*

Control of severe tetany with A.T. 10. The dosage from December 14, 1936, to March 27, 1937, is the amount ordered but, as mentioned in the text, the amount taken is uncertain. The period from March 27, 1937, to May 14, 1937, is omitted because of the uncertainty of dosage, the patient being away at this time. Larger doses of A.T. 10 than those given subsequently were ordered during this period. The blood calcium August 24, 1937, was normal while the patient was daily taking 3.5 cc. of A.T. 10. Note the gradual fall of blood calcium as the dose of A.T. 10 was diminished. The latter figures are probably reliable.

or calcium regularly; the blood calcium had dropped to a little more than 6 mg. per 100 cc.; Chvostek's sign was positive and there were minor tetanic symptoms.

Comment. Although this patient refused to co-operate, it is to be noted that the value of her blood calcium was normal for the first time and remained normal on a daily dose of about 1.5 cc. of A.T. 10. Although we cannot prove it, the patient assures us that she actually did take the required dosage at the time her blood calcium was

cause of recurrence of the hyperthyroidism. Following this a low metabolic rate developed, without much clinical evidence of myxedema. At the same time she had mild tetany. The blood calcium varied between 6 and 7 mg. per 100 cc. This was easily controlled by administration of calcium and parathormone. In 1935 the patient had a transplant of parathyroid tissue culture (Fig. 2), with no lasting benefit, although it seemed that for about two or three weeks she was able to get along without calcium

and with no symptoms of tetany. Since that time the patient has controlled her tetany easily with calcium lactate, taking about 5 teaspoonfuls daily. At other times she was given 40 drops of viosterol without much apparent help. The value for the blood calcium ranged from 8 to 9 mg. per 100 cc. In 1936, A.T. 10 was started and the calcium was discontinued. The blood calcium rose to slightly over 10 mg. per 100 cc. Treatment was continued intermittently until April 8, 1937. At this time she was taking about 120 gr. of calcium lactate by mouth over 4 mg. A.T. 10 was discontinued, and the patient's blood calcium returned to a normal level in about one week. Her symptoms disappeared. Since that time the patient has been taking 0.5 cc. three times weekly with 60 to 120 gr. of calcium lactate daily.

Comment. This patient seemed to get along satisfactorily without any unusual rise in blood calcium on 0.5 cc. of A.T. 10 daily. She was advised to return more frequently for a check-up examination and for determination of blood calcium but neglected to do so, and without

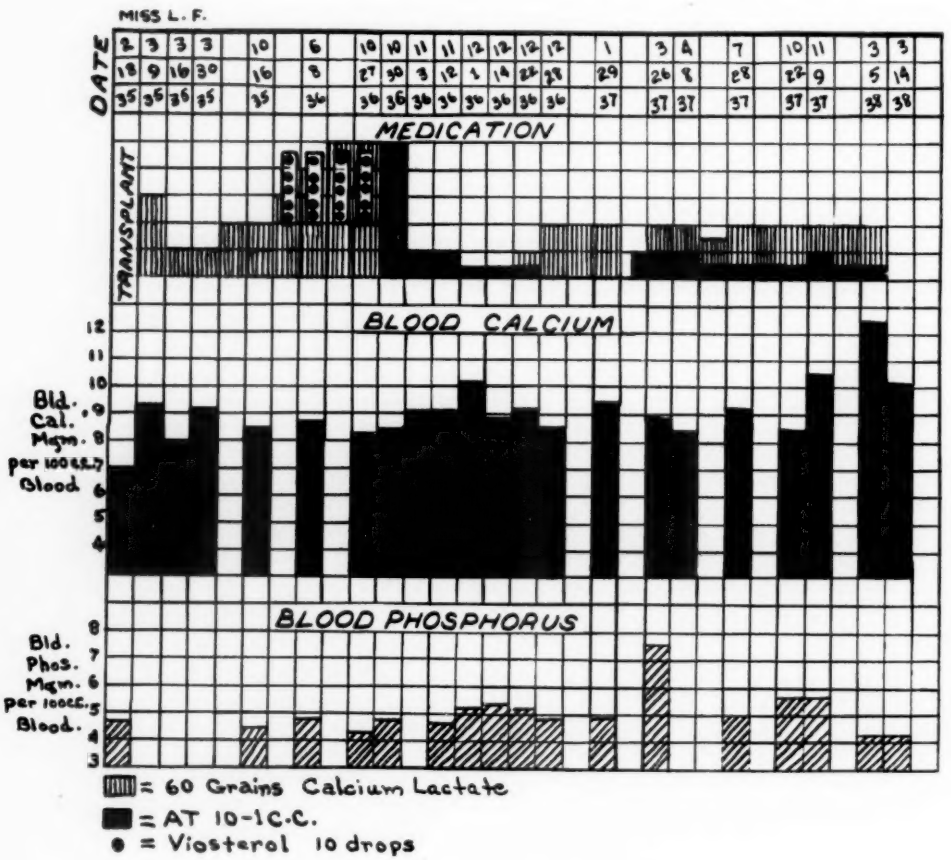

FIGURE 2. *Case 2.*

Control of mild tetany with A.T. 10 and development of hypercalcemia. The value for the blood calcium on February 18, 1935, was 7 mg. per 100 cc. after the patient had been ordered not to take calcium for some time preceding a transplant of parathyroid tissue culture. On October 30, 1936, A.T. 10 was begun and calcium by mouth was omitted. The level of the blood calcium finally rose to 10, the highest it had ever been. From November 9, 1937, to March 5, 1938, the patient took approximately the same amount of calcium daily, with 0.5 cc. of A.T. 10. On March 5, 1938, symptoms associated with hypercalcemia were present.

and 0.5 cc. of A.T. 10 daily. This kept her free from symptoms although the level of blood calcium averaged between 8.5 and 9 mg. per 100 cc. For a short while in November the patient took 1 cc. of A.T. 10 a day and then reduced the dose again to 0.5 cc. daily. She continued this until March 6, 1938, before coming in for a check-up examination. At this time she reported because she felt ill. She had nausea and vomiting, loss of appetite, headaches, pain in the eyes and stated that she never wanted to see calcium again as long as she lived. The blood calcium at this time showed definite hypercalcemia, the level being 12.4 mg. per 100 cc.; the blood phosphorus was slightly increasing the dose, hypercalcemia resulted. This illustrates the necessity for frequent determinations of blood calcium. This patient could easily get along without A.T. 10, since the tetany could be controlled with calcium lactate, but she preferred to take it, stating that she has fewer ups and downs when so doing.

Case 3. This 26-year-old woman entered the clinic in February, 1935. She had had a subtotal thyroidectomy elsewhere in July, 1928, following which she immediately showed evidence of parathyroid tetany which was partially relieved by giving calcium and thyroid extract.

Since then she had complained of stiffness in her fingers. Six months following operation the patient had a convulsion during which she became unconscious for about fifteen minutes. From that time until her admission to the clinic she had had four such attacks. At the onset of these attacks the patient cried out, fell and often injured herself. The last attack occurred one week before her admission.

The patient came to us mainly to find out if it were safe for her to be married because the grandmother of her fiancé had had similar seizures.

was again given and also A.T. 10 in a dose of approximately 3 cc. a week. Pregnancy progressed without complications, but on this dose, without taking calcium, the level of blood calcium fell from 9.1 to 7.8 mg. per 100 cc. She was then given more calcium, and the dose of A.T. 10 was increased to 1 cc. a day for a month before delivery. She had no further trouble and gave birth to a normal, healthy child. The patient was given calcium gluconate intravenously just before delivery and the doses of calcium and A.T. 10 were increased for a few days after delivery,

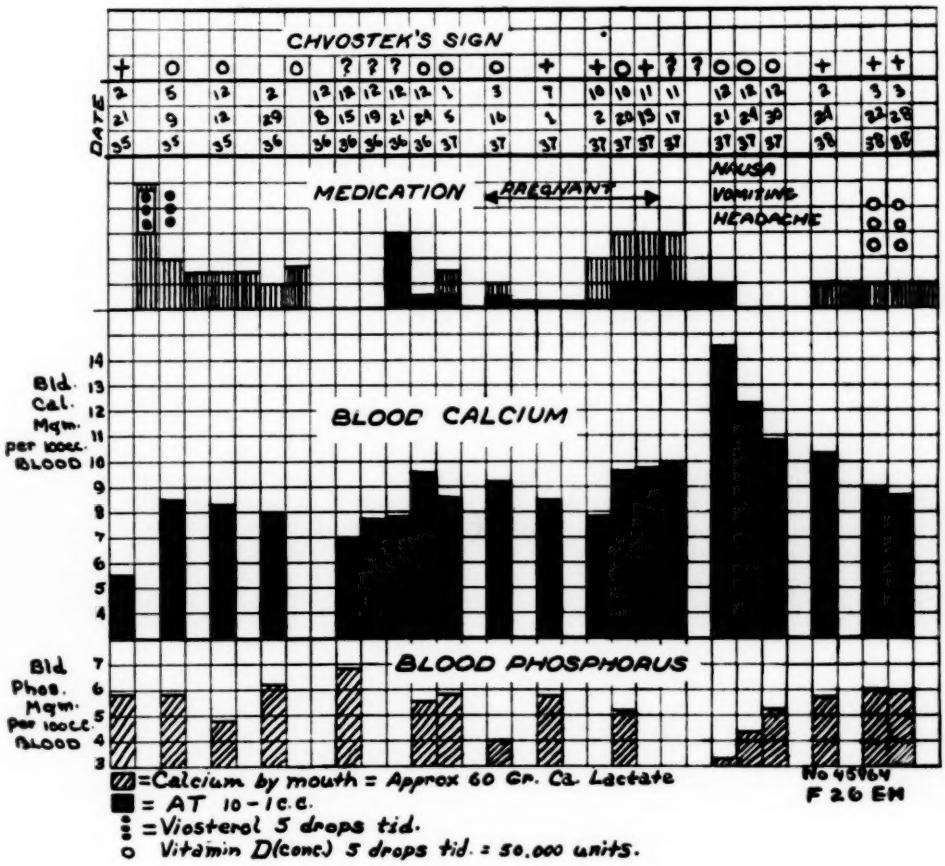

FIGURE 3. *Case 3.*

Course during pregnancy of a patient with tetany, taking A.T. 10; subsequently hypercalcemia developed. The blood calcium determinations and dosage of A.T. 10 are shown in solid blocks. Note the level of the blood calcium on December 24, 1936, after A.T. 10 was begun, also the gradual drop of blood calcium during pregnancy with 0.5 cc. of A.T. 10 daily. Note also the high level of blood calcium which developed one month after delivery while the patient took 1 cc. daily with no calcium by mouth. Of interest is the low value for the blood phosphorus at this time.

The level of blood calcium was found to be 5.7 mg. per 100 cc., and that of the blood phosphorus 5.8 mg. (Fig. 3). She was given viosterol and calcium lactate; this therapy raised the level of the blood calcium, and her symptoms were immediately controlled. On December 8, 1936, all calcium was discontinued for a period of eleven days. The blood calcium averaged 7.5 mg. per 100 cc.; her fingers felt stiff, and her face tingled. A.T. 10 was then given, 3 cc. the first day and 0.5 cc. daily thereafter, with a rather prompt rise in the value for the blood calcium to over 9 mg. per 100 cc. She discontinued A.T. 10 and resumed calcium until she became pregnant. Calcium with the idea of preparing her for nursing her child. When she left the hospital the level of the blood calcium was 10 mg. per 100 cc., and she was advised to continue with 1 cc. of A.T. 10 daily. She failed to come in for over a month at which time nausea, vomiting and headache developed. The blood calcium was found to be 14.3 mg. per 100 cc. The blood phosphorus was very low, and as A.T. 10 was discontinued, the value for the blood calcium fell toward a normal level and the blood phosphorus returned to its previous level. Since that time the patient has been on calcium lactate by mouth and vitamin D concentrate, equal to 50,000 units of vitamin D daily. This

has kept her symptoms controlled; the blood calcium has varied between 8.5 and 9 mg. per 100 cc. It would seem that during pregnancy, on a dose of approximately 3 cc. of A.T. 10 weekly, the blood calcium gradually fell.

Case 4. This 42-year-old woman was operated on elsewhere in 1917 for exophthalmic goiter. She was first seen in the clinic in 1926 and said that she had had severe tetany ever since her operation. She had been treated with calcium and other preparations but had never been free from tetanic seizures. Merely rising suddenly from a chair would throw her into severe cramps. She suffered frequently from laryngeal spasm. From 1926 until 1936 she was treated in the clinic with calcium and, at times, parathormone. She had two transplants without permanent effect; one, a transplant of a parathyroid tumor from a patient with hyperparathyroidism, and the other, a transplant of a parathyroid tissue culture. For about a month after each operation her symptoms were ameliorated. She was started on A.T. 10 on November 20, 1937; 3 cc. was given daily for five days, and then 1 cc. daily thereafter. Calcium was discontinued. At the time A.T. 10 was started, the level of the blood calcium was 9.3 mg. per 100 cc., and that of the blood phosphorus 8.3 mg. Only calcium lactate had been administered before this blood sample was taken. This, incidentally, was the highest value for blood calcium which had been recorded for some time. Before treatment was begun in the clinic her blood calcium had varied between 4.5 and 5.6 mg. per 100 cc., and at the time of the tissue-culture transplant, when she was allowed to go without calcium, the blood calcium went down to 4.8 mg. and the phosphorus to 6.3 mg. The patient continued with A.T. 10 until December 5, 1937. During that time she had taken no calcium by mouth and the blood calcium was reported to be 9.3 mg. per 100 cc., and the blood phosphorus 8.3 mg.

The patient felt much better, and on December 19 she had had no spells whatsoever and was taking 1 cc. of A.T. 10 daily. The value for the blood calcium at this time was 9.5 mg. per 100 cc. The dose was reduced to 0.5 cc. daily, which she continued to take until January 2, 1938, when the blood calcium was 8.6 mg., and the blood phosphorus 5.2 mg. She continued to have no further attacks and took no calcium. On January 25 the blood calcium reading was 7.7 mg., and the phosphorus 5.5 mg., and she was advised to take calcium lactate again, a heaping teaspoonful three times a day. In April, 1938, the blood calcium was 8.6 mg., and the phosphorus, 4.8 mg. She was taking 0.5 cc. of A.T. 10 every day and a level teaspoonful of calcium lactate three times a day. In June, 1938, the first seizure appeared. The blood calcium levels at this time were 8.5 mg. and 6.8 mg. on two separate occasions. From that date until December, 1938, she was not able to purchase A.T. 10, and the blood calcium gradually fell to 7.6 mg., with further seizures. Since then she has resumed A.T. 10 with complete relief and the blood calcium is maintained above 9 mg. per 100 cc. Her blood pressure has gradually risen until, when last seen, it was 210/140; the blood nonprotein nitrogen was 24 mg. per 100 cc., and the renal output 20 per cent of phenolsulfonephthalein in 30 minutes.

Comment. A.T. 10 controlled the symptoms of this patient for the first time in 10 years without calcium, and its effect in this case has been most gratifying.

Case 5. A 37-year-old woman was operated on in May, 1935, for recurrent hyperthyroidism. Mild parathyroid tetany developed on the day she left the hospital. She was given 60 gr. of calcium lactate a day. The level of the blood calcium was 5.7 mg. per 100 cc. Chvostek's sign was positive. Viosterol (15 drops a day) was administered. Later she said that she had received parathormone on several occasions. Her symptoms finally were fairly well controlled on 3 heaping teaspoonfuls of calcium lactate, three times a day, and 20 drops of viosterol. The value for the blood calcium was 7.5 mg. per 100 cc., and that of the blood phosphorus 4 mg.

On December 15, 1936, the blood calcium was 7.1 mg. and the phosphorus 3.8 mg. Calcium was discontinued and A.T. 10 started, 5 cc. the first day and 5 cc. the second day, then 3 cc. for several days and finally 1 cc. daily. She did not take calcium, and when seen two weeks later the blood calcium was 7.4 mg., and the phosphorus 4.8 mg.; she felt improved.

In January, 1937, the calcium was 8.9 mg. per 100 cc.; she was taking 1 cc. of A.T. 10 daily. In June, 1938, the blood calcium was 8 mg., and the phosphorus 3.6 mg.; she had been taking 1 cc. daily. The patient has also taken ½ gr. of thyroid extract daily. She has never taken calcium since using A.T. 10 but has been advised to do so. We have been able to follow her through the courtesy and co-operation of Dr. Charles J. Ashwarton, of Providence, Rhode Island.

Case 6. This 32-year-old woman was first seen in February, 1926. Operation was performed for exophthalmic goiter in July, 1926. Tetany after operation was controlled with calcium by mouth. The patient was seen October 14, 1936, at which time the value for the blood calcium was 9.3 mg. per 100 cc., and that for the blood phosphorus 5.5 mg. She was ordered to take no calcium for 4 weeks, and had few symptoms during that time. Chvostek's sign was positive; the blood calcium was 8.8 mg., and the phosphorus 5.1 mg. She was given A.T. 10, 3 cc. a day for five days, at the end of which time the blood calcium was 9.3 mg., and the phosphorus 5.0 mg. The dose was reduced to 1 cc. daily for five days, when the blood calcium was 10.2 mg., and the phosphorus 4.8 mg. The dose was further reduced to 1 cc. three times a week. The blood calcium then was 9.2 mg., and the phosphorus 5.2 mg.; Chvostek's sign was negative. She has been subsequently free from symptoms.

CONCLUSION

The use of A.T. 10 is an effective and convenient method of controlling severe tetany. While it is probably desirable to use it in all cases of tetany, milder cases can be controlled symptomatically with calcium lactate.

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THE TREATMENT OF SEVERE CARBUNCLES BY X-RAY

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THE treatment of inflammatory lesions by x-ray is not of recent origin. Its use, however, in the treatment of carbuncles, either alone or as an adjuvant of surgery, has not been accepted so generally as would seem to be warranted.

Dunham[1] as early as 1916, reporting 67 cases of carbuncle treated by x-ray wrote, "Nothing in all roentgen therapy gives such positive and uniformly perfect results as the treatment of a carbuncle."

This optimism has been shared by roentgenologists these many years, although publication of detailed data on the subject has been infrequent. Coyle[2] in 1906 described 3 cases of carbuncle treated by x-ray. Dunham's cases appeared a decade later. Almost another decade passed before Hodges[3, 4] in 1924 and 1925 stimulated interest anew in the roentgen method of treating carbuncles. Light and Sosman[5] in 1930 analyzed 50 cases treated by x-ray, stating that the addition of the roentgen ray to the therapy of carbuncles gives promise of being perhaps the most valuable innovation of the past century.

Morton and Leddy[6] in the same year compared the results of early and late x-ray treatment of 26 cases, reporting analgesia, abortion and prompt improvement in those treated early. Similar results in 56 cases were observed by Firor[7] and by Whitmore[8] in 1935, the latter reporting 19 cases treated by x-ray, with a review of the literature.

King[9] in 1937 published the results of 33 cases of carbuncle treated by roentgen ray. The locations were as follows: 12 on neck, 8 on face, 4 on axilla, 5 on extremity and 4 on back. Of this series 3 cases were complete failures. Two of these were seen early, but in both the carbuncle was on the back of the neck and of the deep type in which the mass appeared to be fixed. Surgery had to be resorted to in each case. The third failure was in a case previously treated by incision, where evidently the infection had been carried down to the deeper structures by surgical procedure. Filtered radiation King found to be far superior.

Other articles, presenting for the most part generalizations, have appeared, but Light and Sosman's[5] comment on the meagerness of the English and American literature on the value of x-ray therapy in the treatment of carbuncles still remains pertinent.

Sir James Paget[10] in his clinical lecture on the treatment of carbuncles indicated what is generally recognized today, that a carbuncle is often self-limited and may disappear regardless of the kind of treatment or with no treatment whatever. Incidentally he condemned the use of crucial incision and carrying it beyond the edges into healthy tissue because it did not prevent the carbuncle from spreading. Ordinary carbuncles on the lip and face, he declared, were no more fatal in those situations than in any other. He referred to what he called carbuncular inflammation of the lip or malignant pustule, which he recognized to be more serious than other types, but gave no adequate description of it. This condition probably represents carbuncle of the lip with cellulitis.

When carbuncle is self-limited, convalescence is brief and assured. This may well account for the reputed success of the variety of surgical and non-surgical methods of treatment described. Lest x-ray therapy be included in these "actively useless" measures, as characterized by Paget, carbuncle in the ambulant patient, a lesion that localizes quickly with little or no systemic reaction and no complicating disease, will not be discussed.

There is question here only of severe carbuncle, if you will, an inflammatory lesion that has spread to the subcutaneous tissue, causing a diffuse infection from which toxic absorption has occurred, presenting a fixed area of induration which later discharges on to the surface by a series of openings or massive slough. Each case presented was hospitalized, and had a systemic reaction characterized by fever and an extensive lesion, complicated in many cases by diabetes, and in some by cellulitis, meningitis or septicemia. Others had such accompanying and debilitating conditions as thyrotoxicosis, psychosis, varicose ulcer, compression fracture, subdural hematoma, mid-thigh amputation, carcinoma of the larynx and cardiac disease.

From 1924 to 1937, inclusive, 130 cases of severe carbuncle were treated in the wards of the Boston City Hospital by x-ray alone or in conjunction with surgery. Ninety-five patients were men and 35 women. One hundred and twenty-six patients were discharged well; 4 died, a mortality of 3 per cent.

The lesions were distributed as follows: pos-

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terior neck, 53; upper lip, 28; lower lip, 7; cheek, 16; chin, 6; back, 7; elsewhere, 13.

From the viewpoint of radiation, these cases fall naturally into three groups. Group 1 comprises 60 patients who received roentgen therapy only with dry dressings and had an average hospital stay of eight and a half days. Group 2 represents 34 cases given x-ray therapy before surgery, the latter consisting of puncture, crucial incision or excision of slough; the average hospital stay was thirteen days. Group 3 includes 36 cases subjected to surgical procedure before roentgen therapy, with an average hospitalization of twenty-one days.

Dry dressings only were prescribed in Group 1, chiefly in an attempt to evaluate the efficacy of the roentgen irradiation. In the treatment of Groups 2 and 3, heat in the form of a poultice or heating pad was also employed. The average number of x-ray treatments given was three. Either medium- or high-voltage filtered radiation was employed, depending on the character of the lesion or the apparatus available at the moment.

A brief description of the four fatal cases follows:

Case 470. The patient, a 52-year-old man, was comatose on admission. An upper-lip lesion had been incised at home by his physician. He received one x-ray treatment but died in 72 hours from meningitis.

Case 711. The patient, a 45-year-old woman, suffering from diabetes, received three x-ray treatments for a carbuncle on the back of the neck, which was incised. Death occurred from septicemia in 7 days.

Case 904. The patient, a 36-year-old man with diabetes, was admitted with a carbuncle of the scalp, which had been incised at home. He presented an extensive cellulitis and a positive blood culture on admission. He received two x-ray treatments, but died 34 days after entrance from septicemia.

Case 1638. The patient, a 60-year-old man with diabetes and a posterior neck lesion, entered with a positive blood culture. He received three x-ray treatments, but died of septicemia 27 days after entrance.

Mitchiner[11] analyzed 240 cases of severe carbuncle admitted to St. Thomas's Hospital from 1928 to 1933. He makes no mention of irradiation. There were 13 deaths, a mortality of 6 per cent. Acute pyemia or septicemia was the cause of death in 11 of the fatal cases. It is more likely to occur, Mitchiner states, if surgical interference is undertaken when the carbuncle is spreading or still unlocalized. Eight of the fatal cases he attributed to this error in treatment. There were 10 diabetic patients in his series, an incidence of 4 per cent and 83 patients with facial carbuncles, an incidence of 34 per cent. "No surgical treatment should be attempted under any conditions," he writes, "in facial carbuncles or those complicating diabetes."

In the groups here reported there were 16 diabetic patients, an incidence of 12 per cent. There were 9 diabetic patients in Group 1, 4 in Group 2 and 3 in Group 3 with 1 death in each group from septicemia. While the numbers are small, they permit us to draw the general conclusion that carbuncle in patients with diabetes is a major hazard, but to challenge the oft-quoted dictum "In diabetes the treatment of carbuncles by x-ray without surgery is contraindicated."

The reason for conservatism in the treatment of facial carbuncle, especially that of the lip, is well known. This location is notoriously unfavorable because of the ever-present danger of extension of the thrombophlebitic process "in two directions: by way of the nasal veins, the superior labial, the angular vein, and its anastomosis with the superior and inferior ophthalmic veins into the cavernous sinus or by way of the anterior facial vein into the general circulation. The resulting cavernous sinus thrombosis, meningitis brain abscess or septicopyemia are almost always fatal."[12]

There were 57 cases of facial carbuncle in our series, an incidence of 44 per cent. All received x-ray therapy alone except four of the upper-lip cases, 1 of which fell in Group 2, and 3 in Group 3; 1 of the latter terminated fatally.

If conservatism should be used in the treatment of carbuncles in this location, one wonders why surgeons insist on the excision of carbuncles elsewhere, blithely dismissing irradiation, when over and over again one sees abortion of many of the early carbuncles and the breaking down and localization of the more advanced lesions following x-ray treatment.

One of the most satisfying effects of the x-ray therapy of carbuncles is the relief of pain. Occasionally it is aggravated for a few hours, but rarely does it persist for more than from three to nine hours. In our series, when the x-ray consultation was early, as in the Group 1 cases, heat in any form was forbidden so as to have a control series. The Group 1 cases affirm the analgesic effect of the roentgenization of carbuncles — a phenomenon well established in other conditions.

Absorption with exudate with little or no scarring was the rule when roentgen therapy was given early. Arrest in the spread of the infection was commonly observed even when the treatment was given relatively late. It seems important, however, to use x-ray early and in small doses.

There is good experimental evidence for the employment of x-rays in the treatment of infections. It has been repeatedly shown that relatively enormous doses of x-ray are necessary to

render bacterial cultures inert, but that organisms in living tissue are destroyed by small doses.

Businco,[13] in a series of experiments performed on dogs inoculated with typhoid bacilli, found that the irradiated abscesses healed within eight days, while the controls took from twelve to fifteen days to disappear. Histologically the favorable action of the roentgen rays resulted in a marked hyperplasia of the connective tissue, forming a mechanical barrier to the infiltrating and necrosing process.

Freund[14] has demonstrated experimentally that inflammatory cells do not migrate to the site of the inflammation but are formed locally from connective tissue cells in the blood vessels. In his cases roentgen irradiation inhibited exudation and decreased the number of inflammatory cells.

Colwell[15] summarizes the modern concept of many investigators of the action of x-ray in inflammatory lesions as follows:

> In localized infection a general consideration of the evidence rather points to a response on the part of the reticuloendothelial system than to leukocyte destruction with consequent liberation of antibodies. This is further corroborated by the fact that chronic infections and more acute infections irradiated in their late stages fail to give the best response. If leukocyte destruction were the most important determining factor, a rapid clearing up of the condition might be expected in the chronic cases: the lack of such reaction perhaps rather indicates local exhaustion of the reticuloendothelial apparatus.
>
> A further point is the necessity for small doses of radiation in the treatment of microbial infections and the observation — which seems established — that heavy dosage inhibits or destroys the protective effect of the reticuloendothelial system.

CONCLUSION

A series of 130 hospitalized cases of severe carbuncle treated by x-ray alone or in conjunction with surgery are presented, with a mortality rate of 3 per cent. There was no death in 57 cases of facial carbuncle treated either alone or chiefly by roentgen therapy. There was no evidence that carbuncle in the diabetic patient was a contraindication to x-ray therapy. The 60 cases treated early by x-ray alone had a shorter convalescence than did the others.

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REPORT ON MEDICAL PROGRESS

UROLOGY

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THE following is a brief summary of the major advances that have been recently made in urology.

PROSTATECTOMY

There are three types of pathologic change which occur in the prostate which cause obstruction to the outlet of the bladder: simple hyperplasia (often called benign hypertrophy); prostatic carcinoma (sometimes combined with hyperplasia); and median-bar obstructions and those due to hyperplasia of the median lobe.

For removal of the simple hyperplasia, enucleation through a transvesical approach (suprapubic prostatectomy) has been widely used for many years. An approach through the perineum (perineal prostatectomy) carries a lower mortality and also makes possible removal of prostatic carcinoma, which is present in about one fifth of all cases. This type of operation has also been standardized throughout many years. For the median-bar and median-lobe obstructions operation through the urethra, in the former by the use of the punch instrument perfected by Young, has been generally very satisfactory. However, because the original instrument made no provision for the control of bleeding, various modifications (Braasch-Bumpus, Thompson) have been produced which employ one form or another of electric current. With the advent of the electrosurgical cutting current this was adapted to a transurethral instrument (McCarthy) by which tissue can be excised with easy control of bleeding. After the perfection of such instruments steps were soon taken to extend their use to cases of prostatic hyperplasia much more extensive than mere enlargement of the median lobe. It was found that this form of operation made few demands on the patient's strength and therefore carried a low mortality. Convalescence also was definitely shortened. Soon transurethral operation was being advocated for all obstructions caused by the prostate regardless of their nature or type. A wave of enthusiasm followed, largely fostered by the industrious over-advertising of instrument dealers, during which many physicians as well as most of the general public were swept off their feet, hoping that this so-called "new" method, so different from the earlier "cutting operations," was in truth a panacea.

Sufficient time has now elapsed to permit an unprejudiced survey of the whole field, such as has been the subject of two strikingly important communications read at the last meeting of the American Medical Association. The first, by Davis, presents an analysis of a nation-wide inquiry addressed to over a hundred urologists. It should be closely studied by the whole medical profession, for though dealing specifically with transurethral resection of the prostate, it also contains many wise comments on "the reaction of the medical profession to anything new." Davis outlines by the use of a graphic chart the succeeding stages of this apparently characteristic reaction.

> Overenthusiasm [he says] inevitably follows the discovery of a new therapeutic agent, particularly that discovery which tends to be startling or which carries with it a dramatic appeal. After overenthusiasm, in varying degree but in definite sequence, come publicity, commercial exploitation, incompetence and abuse, followed by poor results, recognition of defects and dangers, fear, decreased use and overcorrection, until finally such merits as may exist become recognized in their true light and the new therapeutic agent (drug or surgical method) reaches stability at its proper level of usefulness.

Davis's conclusions are of course that removal of the prostate by the transurethral route is far from being a panacea. About 80 per cent of urologists believe in adapting the form of operation to the conditions presented by the patient. "A skillful few, however, rather than fit the operation to the patient have succeeded in fitting the patient to the surgeon."

One point which comes clearly out of a present-day study of the transurethral method is that it is distinctly *not* an operation to be done by the occasional operator, for all good or even passable results depend on a most exact and extensive familiarity with the bladder outlet and the changes caused in it by the various types and forms of prostatic hyperplasia, as well as on a high degree of manipulative skill. Such familiarity and experience can only be acquired by those relatively few urologists who are associated with a large clinic.

The second communication on this subject is that of Hinman. After discussing the three types

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of obstruction to urination by the prostate, — median bar, hyperplasia and cancer, — he points out that of the three methods of surgical approach — the suprapubic, perineal and transurethral — the perineal alone enables a logical attempt to be made toward the entire enucleation of malignancy. Since cancer of the prostate is the underlying cause of the prostatism in about 1 case out of every 5, a strong argument in favor of the perineal approach exists. As to the relative claims of each of the three methods of attack, Hinman says that the suprapubic approach is suitable for hyperplasia, and is rarely if ever used for removal of a median bar or for cancer except unintentionally when the neoplasm is concealed within hyperplasia. The surgical risk is high, the mortality being between 4 and 20 per cent, with an average of 8 per cent. The period in the hospital is relatively long — from thirty to forty days. As a rule the functional results are both good and permanent.

The perineal operation is difficult to master, and the functional risk in the hands of the inexpert surgeon is high. The hospital stay averages twenty-one days. The risk is low, the mortality being between 1 and 8 per cent, with an average of 3 per cent. Also, this is the only operative approach which results in the cure of cancer.

The transurethral approach, according to Hinman, is most popular and its greatest fault lies in its very popularity. The mortality varies from 1 per cent in the hands of the expert to as high as 30 per cent or more. The average mortality is probably about 4 per cent. Even when the operation is well done, recurrence is frequent, and of course no attempt is made by this procedure to control cancer.

At the clinic of the Peter Bent Brigham Hospital we have been convinced for at least a decade that the approach to the prostate through the perineal route is by far the most logical one, and is followed by the best results as regards both function and mortality. Especially is this true in cases in which the prostate is carcinomatous, for when the gland is thus exposed, accurate judgment of the extent and position of the malignancy becomes possible. Because of the customary late recognition of prostatic cancer it is often impossible to excise all the malignancy, even by a total prostatectomy. But by the entirely adequate exposure through the perineum it is always possible to free the outlet of the bladder by excision of the growth in this region, after which radon seeds can be used in those areas which cannot be removed. Progressive growth of the carcinoma after such a palliative operation is often quite slow, patients not infrequently retaining good general health and a satisfactory bladder function for from two to four years.

The transurethral operation in our hands has been confined for the most part to benign median-bar and middle-lobe obstructions and to benign hyperplasias of lateral and median lobes of such size that a complete enucleation of all hyperplastic tissue seemed possible at a single operative session. It has been well recognized, ever since the earlier days in which the electrocautery of Bottini was used, that the removal of tissue in the floor of the prostatic urethra in the form of a gutter or groove is entirely inadequate: the bladder cannot be completely emptied, infection persists or increases and the patient is not cured. Therefore a transurethral attack on a hyperplastic obstructing prostate cannot be conscientiously adopted by the surgeon unless he is certain that he will be able to remove practically all the hyperplastic tissue. It is largely due to a lack of appreciation of this need that we have seen so many poor results after an attempted resection through the urethra. For to remove the necessary amount of tissue of the larger glands requires an extensive and complete familiarity with the prostatic portion of the urethra and the changes in its appearance caused by the hyperplasia. This demands good vision at all stages of the operation, to be obtained only by adequate control of bleeding. The Braasch-Bumpus punch, seen in its latest form in the instrument of Thompson, is doubtless the best in that there is no devitalized or cauterized tissue left after operation to act as a frequent cause of late bleeding on the separation of the sloughs. The proper use of this instrument requires much practice, however, especially by those surgeons who have not had experience in vision through an instrument devoid of lenses. The McCarthy instrument, in which the cutting is done by an electric current of high frequency, is easier to use on the whole, but because the character and modalities of the electric current with its especial generator must be accurately adjusted, one finds only too often difficulty in controlling bleeding or in cutting cleanly without causing cauterization and its attendant dangers from secondary hemorrhage.

Everyone familiar with the present developments of the transurethral operation must appreciate that in spite of its failures and shortcomings in the past, it represents in proper hands today one of the outstanding accomplishments of urology. In reality, the only remaining difference in opinion lies in the decision as to what types of obstructing prostate should be so attacked. This aspect would seem to be most adequately covered by the summary of Davis above quoted, in which

it was found that the large majority of surgeons practice careful selection of the cases which in their hands seem suited to transurethral surgery.

In summary, therefore, present-day opinion may be stated as follows:

(1) Suprapubic prostatectomy is technically simple. It is probably the only type of operation which should be undertaken by the occasional surgeon. Its mortality is higher than after other types of operation, and the convalescence longer, but its results in general are both good and permanent.

(2) Perineal prostatectomy is technically exacting on the surgeon but less so on the patient. It should not be undertaken without a detailed familiarity with the anatomy of the perineum, which can be acquired only by extensive experience. Its mortality is very low, and it is the only route by which carcinoma can be adequately controlled. It is the operation of choice in many clinics.

(3) The transurethral operation, though seemingly simple, is in reality harder to execute than either of the other forms when applied to obstruction by the prostate caused by factors other than hypertrophy of the middle-lobe or median bar. Its indiscriminate use has doubtless done much harm, which to some extent has obscured its real worth. It entirely omits from consideration the important and frequent cases of prostatic cancer. A second operative session is quite often necessary. The procedure carries a very low mortality and short convalescence, but its results are invariably poor unless all or nearly all the hyperplastic tissue is removed and hemostasis is accurately and completely obtained. In order to achieve this result an extensive training is imperative.

UNILATERAL RENAL DISEASE AND HYPERTENSION

The association of various forms of renal disease with general circulatory hypertension has long been of much interest to clinicians. Intrinsic renal disease of a diffuse type, as in vascular nephritis and pyelonephritis, is commonly accompanied by hypertension at some period in the progress of such disease. The general belief in the past, however, has been that a bilateral renal abnormality must exist in such cases. Recently work which has accumulated from experimental laboratories has demonstrated beyond question that arterial hypertension can be produced in animals by various methods which interfere with the renal blood supply of only one kidney. The most generally successful method has been that of Goldblatt, who has devised a clamp by which partial constriction of the renal artery can be made. As a result of the ischemia produced by such a clamp a persisting hypertension appears, even though one kidney is allowed to remain normal. Following removal of the occluding clamp or excision of the kidney so treated, the blood pressure returns to normal.

This is not the place to undertake a discussion of the considerable volume of work which has been devoted to this subject, nor of the present attempts to describe the cause of the hypertension so produced. The important aspect for the urologist lies in the clear demonstration of the fact that such hypertension can be present even in unilateral renal disease. For if cases of this kind are to be found in the clinic, it is fair to assume that cure of the vascular manifestations may follow a nephrectomy. This has in fact been found to be so, and during the past year several papers have been published in which such cases are described. Leadbetter and Burkland's case was that of a colored boy of five and a half years who had had hypertension from the age of six months. There was enlargement of the heart and an ectopic right kidney, without evidence of infection. The average blood pressure was about 152 systolic, 90 diastolic. There were no abnormalities of the eye grounds. After nephrectomy, at which the ectopic kidney was found alongside the right iliac artery, the blood pressure fell immediately to 125 systolic, 92 diastolic, and after discharge it was 96 systolic, 70 diastolic. Examination of the kidney showed no evidence of infection, but the lumen of the renal artery was almost occluded by a tissue plug made up of smooth muscle, considered by the authors to represent an anomaly of development.

Six cases of hypertension in the presence of unilateral renal lesions of the infective type are related in the communication of Crabtree. In all there was hypertension which fell noticeably after nephrectomy. Boyd and Lewis report a further case in which the blood pressure became normal after nephrectomy for renal infarct.

It appears that in view of this undoubted close relation between certain renal conditions and the phenomena of general vascular hypertension, all patients should be investigated by detailed urological methods before being subjected to any one of the various forms of surgical operation designed to relieve their hypertension, such as sympathectomy, section of anterior nerve roots and adrenal denervation.

RENAL INFECTIONS

Progress in the control of renal infections has been made along several lines during the last year or two. It is generally known today that each case of infection must be closely studied in order

to determine and remove the source or cause of such infection if possible. Of equal importance is the demonstration of the presence or absence of any factor in the urinary tract which may act to cause stasis. Only after removal or correction of such mechanical cause can one hope to combat successfully the attendant infection. For instance, it is practically impossible to bring about sterilization of the urine when a kidney bears a stone, or when the stone lies in the ureter and thus causes stasis in the passages above it. After such a mechanically obstructing cause has been removed or proved to be absent, the infection can be fought by one or another of the various antiseptic substances, especially mandelic acid or sulfanilamide. Also, it is to be again emphasized that the criterion of cure of any urinary infection should always be a sterile culture of the urine drawn under aseptic precautions, for it has been shown repeatedly that the absence of pus cells and of symptoms is not enough. Treatment must be continued till the urine is sterile, in order to avoid recurrence.

In a recent article Braasch discusses this subject. He first notes the three types of pyelonephritis. The first (the so-called "acute pyelitis" of earlier days), coming as an acute attack of relatively short duration, is very common, possibly standing next in frequency to the infections of the respiratory tract. He writes:

> The medicine we give these patients is often given credit for clearing up infection which in reality has been overcome by natural resistance. However, when the infection persists longer than four or five days and when it is accompanied by fever and chills, nature is materially aided by the administration of any of the various chemotherapeutic agents now available.

The second type is characterized by recurring attacks of acute infection lasting possibly several weeks and reappearing after variable lapses of time. In practically all such cases, though the patient seems well, the urine does not become sterile between attacks, and some mechanical condition in the urinary tract which induces stasis may be present.

The third type of pyelonephritis is its chronic form. Braasch includes under this heading those cases in which the infection has persisted for at least a year and in which, with rare exception, both kidneys are involved. He notes that when only one kidney is found to be infected over a long period of time, a secondary complication should be assumed, usually requiring surgical treatment. Though some patients may acquire a relative immunity to such infection, in others secondary complications are common, such as stone formation, hematuria or pyonephrosis due to a cicatricial deformity.

Of the two drugs today most potent in fighting such infections, mandelic acid is of most use in infections caused by *Streptococcus faecalis*. This drug is usually only effective when the urine is made highly acid by the administration of ammonium chloride, and this condition may be difficult or impossible to bring about. Sulfanilamide is particularly efficient in combating urinary infections due to the colon bacillus and the proteus bacillus. Braasch believes that there is no doubt that sulfanilamide and its derivatives have already reduced the occurrence of chronic pyelonephritis and even bid fair to eliminate it. He finds that large doses of sulfanilamide are frequently unnecessary in infection of the urinary tract, and that small doses — sometimes as little as 1 gm. daily, given continuously — are of distinct value.

With the increasing efficacy of chemotherapy it may be predicted that primary pyelonephritis will ultimately be largely limited to its acute and subacute stages and that chronic infections will develop only occasionally.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25221

PRESENTATION OF CASE

A fifty-four-year-old married Italian shoemaker was admitted complaining of abdominal swelling and edema of the legs.

Four years prior to admission the patient noted a gradual darkening of his skin and at the same time a progressively increasing shortness of breath following mild exertion. One year later he began to suffer from a dull nonradiating pain in his right side just under the costal margin. Eight months before entry his ankles became swollen each evening but were normal in the morning. During the succeeding four months the swelling gradually extended upward to the knees, thighs and genitalia. His abdomen then became enlarged quite rapidly. The pain in the right upper quadrant became more severe. He rapidly lost weight and strength and could no longer work. Dyspnea increased and severe orthopnea developed. At about this time he first noted the presence of small amounts of bright-red blood in his stools and felt a small mass at the anus following defecation. His physician gave him arm injections and did about fifteen abdominal taps at weekly intervals. At each tap "about two bucketfuls" of fluid were removed. He had had neither melena, hemoptysis nor diarrhea. There was no pruritus, and he had noted no change in the color of his eyes. He denied the use of alcohol in any form. Appendectomy and cholecystectomy had been done at some unknown period in the past.

Physical examination showed a cachectic moribund man with marked ascites and edema of the legs. The skin was deeply bronzed and the sclerae appeared to be jaundiced. There was no pigmentation of the buccal mucous membrane. Over the neck and chest there were a few spider-like telangiectases. The neck veins were full and showed visible pulsations. There was marked clubbing of the fingers. Examination of the chest showed subcrepitant rales over both lung bases posteriorly. The lungs were resonant throughout except for slight dullness at the right base posteriorly. Examination of the heart was negative. The blood pressure was 96 systolic, 60 diastolic. The abdomen was distended, and a fluid wave was elicited. The superficial veins were dilated, and extended up over the chest. Prominent veins were also evident in the axillary regions. A firm, nodular, slightly tender liver edge was palpated 2 cm. below the right costal margin, extending from the right midclavicular line to the xiphoid process. No other organs or masses were palpable. The genitalia were edematous. Rectal examination revealed tender hemorrhoids. The reflexes were sluggish but equal.

The temperature was 99.5°F. rectally, the pulse 110, and the respirations 30.

Examination of the urine showed a specific gravity of 1.026, a red test with Benedict's solution (following intravenous glucose), 5 to 8 white cells and 10 to 20 red cells per high-power field, no albumin, no bile and no casts. The test for urobilinogen was positive in dilution of 1:40, and doubtful at 1:80; a normal control was positive at 1:20 only. No acetone bodies were present. The blood showed a red-cell count of 3,480,000 with 81 per cent hemoglobin, and a white-cell count of 10,640 with 91 per cent polymorphonuclears. The hematocrit was 36.3. The nonprotein nitrogen of the serum was 21 mg. per 100 cc., the protein 5.9 gm. and the van den Bergh 1.5 to 2.0 mg. of bilirubin, diphasic. The fasting sugar on whole blood was 141 mg. per 100 cc. A capillary sugar tolerance test showed a fasting blood sugar of 84 mg. per 100 cc., after a half hour 118 mg., after one and a half hours 174 mg., after three hours 240 mg., after four hours 244 mg., and after five hours 194 mg. The fasting blood sodium was 137 milliequivalents per liter. The bleeding time was 2½ minutes, the clotting time 13 minutes; the clotting began in 6 minutes. A blood Hinton test was negative. A bromsulfalein liver function test showed 0 to 5 per cent retention. A Takata-Ara test was strongly positive. A formol-gel test was positive and indicated that the globulin was approximately 5 per cent. Several stool examinations were guaiac negative. An electrocardiogram showed a P-R interval of 0.14 seconds, normal rhythm, flat T_1, low T_2, T_3 and T_4, and low voltage in the QRS complexes. A special stain on a skin biopsy was negative for iron. An abdominal paracentesis yielded 8000 cc. of clear, straw-colored fluid with a specific gravity of 1.008.

An x-ray film of the chest showed scarring of both apices and a fine miliary mottling involving the entire lung, being particularly marked in both lower lung fields where there was questionable confluence of some foci. The mottling seemed to have a bronchial distribution. Emphysematous blebs were thought to be present bilaterally but were particularly evident in the left upper lung field. The heart shadow was not remarkable.

On the second hospital day, before intravenous

glucose had been given, the urine showed a yellow test with Benedict's solution. On the fifth hospital day 5000 cc. of clear, light amber fluid was removed from the abdominal cavity by paracentesis; the specific gravity was 1.008. His condition grew progressively worse, and the abdomen rapidly refilled. On the twelfth hospital day 5000 cc. of straw-colored fluid was again removed. The patient refused to take food. His temperature remained essentially normal; the pulse was about 100, and the respirations 20. He gradually failed, and died on the eighteenth hospital day.

Differential Diagnosis

Dr. John H. Talbott: The first time that I read this record the diagnosis was fairly obvious, the second time not quite so obvious, and at the third reading I was thoroughly convinced that the house staff probably puzzled as much over the diagnosis as I have. The patient was fifty-four years of age and an Italian. Dr. Wyman Richardson has called our attention to the fact that cirrhosis of the liver is common in Italians. The patient's first symptom, darkening of the skin, was noted four years prior to admission. Pigmentation of the type described may be observed in four or five different diseases. The first dyscrasia that one thinks about is Addison's disease. Undoubtedly the physicians in charge of this man thought very seriously of a diagnosis of Addison's disease for they requested a serum sodium determination. The concentration was 137 milliequivalents per liter. This is a relatively normal value. I do not believe this patient had Addison's disease in spite of the fact that there was some hypotension and pigmentation of the skin. It is specifically stated that there was no pigmentation of the mucous lining of the mouth. If this patient had had chronic Addison's disease as opposed to acute adrenal insufficiency, he should have had pigmentation in the mouth. At the present time I am not justified in making a diagnosis of chronic Addison's disease without it.

The pain in the right upper quadrant is at least consistent with cirrhosis of the liver. When I use the term cirrhosis of the liver I mean "sclerosis" without etiologic implications, at least not until I summarize the case. There may be sufficient pain from cirrhosis of the liver to warrant surgical consultation, and not infrequently surgical intervention is advised. The anal mass was probably due to hemorrhoids. The small amount of bright-red blood in the stools confirms this impression. The patient was tapped fifteen times before admission and three times afterward. Recurring ascites is not in itself diagnostic as there are several conditions that may require frequent tapping. The injections in the arm were possibly Salyrgan, which is an effective diuretic.

The patient denied the use of alcohol. We do not hesitate, however, to make a diagnosis of alcoholic cirrhosis of the liver in a patient who has a similar negative history. Patients who consume alcohol frequently will not give a correct story.

The skin was deeply bronzed. This is significant. In hemachromatosis or "bronze diabetes," pigmentation of the skin is characteristic. The pigmentation is a blue slate or lead color in contrast to the silver sheen of argyria. In Addison's disease the pigmentation is brown without a metallic tinge.

There were a few spider telangiectases. This is consistent with the diagnosis of intrahepatic disturbance, and nothing more.

The neck veins were full and showed visible pulsation. I should like to attribute these to ascites, and shall not discuss them further.

There was marked clubbing of the fingers. That is an interesting finding. Four or five years ago Dr. Francis M. Rackemann asked me to see a patient with clubbing of the fingers, some respiratory disturbance and unsaturation of the arterial blood. I raised the question of congenital heart disease. Three years later the patient died from cirrhosis of the liver. The oxygen unsaturation which accompanies cirrhosis of the liver is something that has been appreciated in the past three or four years only. Snell[1] at the Mayo Clinic found that 50 or 60 per cent of the cases of cirrhosis of the liver had a saturation of the arterial blood as low as 80 per cent. We occasionally see patients with cirrhosis of the liver who have clubbing of the fingers. I wonder whether the oxygen unsaturation we see frequently associated with cirrhosis of the liver may not be the mechanism of the clubbing of the fingers, which is only infrequently observed in this disturbance. This may be associated with a dysfunction of hemoglobin formation. It is possible that a change in the nature of normally occurring hemoglobin may be the precursor of the pigmentary changes that we see in hemochromatosis, which only rarely follows cirrhosis of the liver. I shall say more about this later.

The question of constrictive pericarditis might be raised, but I think it can be dismissed without further discussion. No spleen was palpable. The patient had ascites at the time they looked for the spleen, and I am wondering if subsequently, after tapping, the spleen was palpable.

The change in the liver is interesting. According to the description the subdiaphragmatic enlargement began in the midclavicular line and went over past the xiphoid process; that is, the

enlargement occurred where a middle lobe might be. Many years ago McCrae and Caven[2] called attention to the fact that syphilis of the liver was frequently associated with left-lobe involvement.

The patient had a positive sugar test in the urine on one occasion before any glucose had been given, and again after it had been given internally. The sugar-tolerance curve is not very convincing. We have been studying sugar tolerance in a good many patients with various disturbances, particularly gout, and frequently we find a curve, quite like this, with prolonged elevation. It may remain elevated as high as 200 or 250 mg. per 100 cc. for three, four or five hours, and we are rather certain that most of these patients do not have diabetes mellitus. Furthermore I do not believe we have anything in the history that justifies our making a diagnosis of diabetes mellitus. The presence of a small amount of sugar in the urine in a patient who has obvious intrahepatic damage can be explained on that basis alone. Lastly, there were no acetone bodies in the urine, and I do not interpret the terminal event as diabetic acidosis and coma.

The blood Hinton test was negative. I mentioned previously that there may be enlargement of the left lobe of the liver in syphilitic cirrhosis, but I hesitate to disregard the negative blood test. I should have been pleased if we had had a Wassermann or Hinton test on the ascitic fluid. That was not done. The bromsulfalein liver test was 0 to 5 per cent retention. This is normal. The Takata-Ara and the formol-gel tests were positive. These are indications of an increase in serum globulin. There has been considerable interest in the past four or five years in the pathologic conditions which are associated with an increased globulin or pseudoglobulin reaction. The three conditions most frequently encountered in which a concentration greater than 4.0 gm. per 100 cc. is observed, are multiple myeloma, lymphogranuloma inguinale and cirrhosis of the liver. The first two I am not going to consider. In the third condition the increase may be a combination of two factors. I have just mentioned that a disturbance of formation of hemoglobin and resulting change in the nature of hemoglobin probably occur in cirrhosis. An increase in globulin may be associated with a related intrahepatic dysfunction. A loss of albumin in ascitic fluid with a stress on the protein-forming mechanism is the second factor.

Should we consider malignancy in this patient? The stool examination was negative for blood. There was no hemoptysis, no hematemesis, and the patient passed no large amount of fresh blood by rectum.

The electrocardiogram is of little help to me.

A special stain was done on a skin biopsy. Apparently they were looking for hemochromatosis. However, we do see patients with hemochromatosis in whom the biopsy is negative. Again, this negative test is of no help. I should have preferred either two or three negatives or one positive.

The abdominal paracentesis yielded a fluid with a specific gravity of 1.008, which indicates a transudate and not an exudate.

The interpretation of the x-ray films of the chest is most unsatisfactory to me. Perhaps Dr. Holmes will help with the diagnosis.

Dr. George W. Holmes: These films show an obvious extensive process involving both lung fields. It is rather generalized, a little more marked at the bases. We have observations on February 6 and on February 13 which show practically no change in the appearance of the chest. Between February 13 and 24, however, there is a very marked change, a difference in the whole character of the picture. It is interesting that his heart is within normal limits both as to size and shape and stays that way, so far as I can determine, throughout the stay in the hospital. He has some tortuosity of the aorta. The whole picture does not seem to be in any way connected with the vascular system. The process itself could be due to a number of diseases. It is not suggestive of tuberculosis but could be due to metastatic malignant disease, to some fungous infection or to one of the unusual forms of peribronchial disease. The terminal picture, I think, is due to edema or pneumonia on top of the previous process. Would you like to have me go farther?

Dr. Talbott: May I ask a question? Does it look anything like a generalized syphilitic lesion?

Dr. Holmes: I do not know of any generalized syphilitic lesion that would look like that.

Dr. Talbott: Could leukemia give a picture comparable to this?

Dr. Holmes: It is very unlikely.

Dr. Talbott: It has been described but we have not been fortunate in seeing it. Possibly we do not consider it so frequently as we should.

Dr. Holmes: That is probably true.

Dr. Talbott: The only symptoms that were referable to the chest were dyspnea and orthopnea. He had no cough or fever at any time.

Dr. Holmes: It seems strange he did not have cough. I should be inclined to interpret that the way you did the story about alcohol. He must have had some cough. I cannot differentiate the things that I have named.

Dr. Talbott: Could it be idiopathic or non-

tuberculous chronic infection with generalized fibrosis?

DR. HOLMES: Yes.

DR. TALBOTT: In the first place, I do not believe that this man died of a lung condition. I believe that he had a cirrhosis of the liver, and that he died of hepatic insufficiency. I am going to spend a little time discussing the various types of hepatic disturbance that he might have had.

He had an enlargement between the right and left lobe. There is little evidence, so far as the abdominal picture is concerned, that he had malignant disease. I cannot believe he had fifteen or sixteen tappings of clear fluid from a malignancy alone. There is little evidence that this is an echinococcus cyst. Against liver abscess is the fact that he had no fever at any time. He may have had fever in the past, but he certainly did not in the hospital. If this is syphilitic cirrhosis, I should like to have more evidence of it in the clinical picture, such as a past history of exposure — but I must admit the past history is not reliable — or signs and symptoms of syphilis elsewhere. If we had seen him earlier in the disease we might have given potassium iodide to note whether he responded to therapy in the way that a patient with syphilitic cirrhosis should. On the evidence at hand I do not feel justified in making a diagnosis of hepar lobatum or syphilitic cirrhosis of the liver. I do not believe that he had diabetes mellitus or that he died in diabetic coma. We have one negative skin biopsy. So far as hemochromatosis is concerned, he had pigmentation and cirrhosis. If he did have hemochromatosis it was of a very mild degree, such as one occasionally sees in patients with cirrhosis of the liver, and had not developed sufficiently to permit a clinical diagnosis or to allow the pathologist to comment on it other than to say that it was a very early form. I might mention acanthosis nigricans, which is associated with pigmentation of the skin. There is little to justify a serious consideration of this diagnosis.

With a negative past history, I do not see how I am able to make a clinical diagnosis of what is going on in the chest. The x-ray films have not helped us except to exclude certain conditions. It is not a very obvious diagnosis and I shall have to leave it undiagnosed. We are then left with the diagnosis of cirrhosis of the liver, which I think was probably alcoholic in origin. I should be more cautious, probably, and call it idiopathic cirrhosis of the liver. I think that he died of hepatic insufficiency.

DR. PAUL D. WHITE: This man came to the East Medical Service while I was visiting. I admire Dr. Talbott's discussion of the case. He has ably expressed our own confusion as we took up one point after another. We tried very hard to make a diagnosis of hemochromatosis but were not successful.

We were very much interested in the relation of the clubbing of the fingers to the pulmonary disease, aside from the possible effect of the cirrhosis of the liver. The statement that Dr. Talbott made about the visible neck-vein pulsation was, I think, very wise. There is no indication, of course, that, with a small and apparently normal heart, cardiac failure would be responsible for such a pulsation. This pulsation was not marked. It can be accounted for, I am sure, by the pressure from a large amount of ascites. Recently, in the past year or so, I have observed a slight jugular pulsation just above the right clavicle even in normal individuals who are very short and whose diaphragms are high. The venous pressure in such cases is normal, even though one can see the jugular pulse.

The electrocardiogram in this case is not particularly helpful. It may mean coronary disease, which need not enter the clinical picture, or a toxic condition and nothing else.

DR. DONALD KING: I saw the x-ray films when this patient was on the ward. We raised the question as to whether this might have been a case of dilatation of the bronchioles rather than of the larger bronchi. The honeycomb lesions shown in the films are much like those which have been present in one or two cases of pulmonary fibrosis with bronchiectasis, and in these cases autopsy has shown marked dilatation of the bronchioles.

CLINICAL DIAGNOSES

Cirrhosis of liver.
Gastric ulcer.
Pulmonary fibrosis.

DR. TALBOTT'S DIAGNOSES

Cirrhosis of liver (? alcoholic).
Undiagnosed lesion in the lungs.

ANATOMICAL DIAGNOSES

Cirrhosis of the liver, alcoholic type.
Pulmonary fibrosis.
Emphysema.
Bronchiolectasis.
Pulmonary edema.
Bronchopneumonia.
Gastric ulcer, active.
Duodenal ulcer, healed.
Ascites.
Arteriosclerosis.
Operative wounds: cholecystectomy and appendectomy.

Pathological Discussion

Dr. Tracy B. Mallory: The autopsy on this man showed as the primary disease a very extensive cirrhosis of the liver. It was atrophic, with nodules of regeneration of considerable size. It was not very clear to us at autopsy why one portion had been so readily palpable. There was no point of particular prominence.

The liver microscopically showed minimal traces of iron but certainly not enough to justify a diagnosis of hemochromatosis. A slight increase in intrahepatic iron is a common thing in cirrhosis of the liver. Chemically it can usually be made out, and histologically it is often seen in cases which are not primary hemochromatosis. In a few places we could find quite typical hyalin of the alcoholic type, although that is an unusual finding in an Italian. The spleen weighed only 150 gm. so it could not have been felt. There were no varices. The pulmonary lesion I cannot name any better than the clinician could. There was an extensive pulmonary fibrosis with some dilatation of the bronchioles and a great deal of intimal thickening in many of the pulmonary arteries. At this late stage of the game it would be difficult to say whether the arterial change was primary or secondary. My guess is that it was secondary, and I should assume that at some time in the past this man had had an extensive focal pneumonitis followed by organization rather than resolution and that all the changes were secondary to that. We could find nowhere anything that suggested pulmonary tuberculosis. What the etiology was, I have no idea.

The upper abdominal pain may of course have been due to the cirrhosis of the liver, as Dr. Talbott suggested. However, he had an active gastric ulcer and the scar of a healed duodenal ulcer as other possible factors.

Dr. White: Was the right ventricle enlarged?

Dr. Mallory: No. The heart weighed only 250 gm.

Dr. Talbott: Was there anything in the kidneys to explain the hematuria?

Dr. Mallory: Nothing of significance — only slight vascular changes.

Dr. Holmes: What was in the lungs to explain the marked change during the period of observation?

Dr. Mallory: Terminal edema and bronchopneumonia.

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CASE 25222

Presentation of Case

A forty-two-year-old housewife was first seen six days before admission to an outside hospital complaining of chills, fever and sore throat of three days' duration.

She had had two chills in the evening lasting from five to ten minutes and her temperature on one occasion was 101°F. She had vomited once. Examination showed a large, swollen, tender area in the left submaxillary region. The left tonsil was swollen and very red. She could not open her mouth more than half way. The temperature was 103.2°F. During the first thirty-six hours she was given 240 grains of sulfanilamide and 60 grains more during the next twelve hours. On the second day after this therapy was begun her temperature was 101°F. and the swelling in the throat had slightly decreased. On the third day her white-blood-cell count was 3400 and the sulfanilamide therapy was promptly stopped. The next day she was prostrated, confused and very cyanotic. The neck was still very tender, but the swelling in the throat had greatly receded. The temperature was 98°F., the white-blood-cell count 30,000. On the following day there was much less prostration and she was no longer confused. The white-blood-cell count was 17,800, temperature 98.6°F. The neck and throat were practically normal. On the sixth day she had a chill lasting a half hour. Soon afterward her temperature was 105°F., pulse 140, respirations 24. She was then admitted to the outside hospital.

Physical examination showed a well-developed and nourished woman whose throat was slightly red, but otherwise normal. Examination of the eyes was negative. There was no glandular enlargement. The chest examination was negative except for a to-and-fro scratching sound over the pulmonic valve area which was thought to be due to her very rapid and forceful heart action. The abdomen was slightly distended but otherwise negative. Neurological examination was negative.

She was given 100 grains of sulfanilamide without obvious effect. A lumbar puncture showed normal dynamics and a clear colorless fluid. Her nonprotein nitrogen was normal. Large doses of sulfanilamide were decided on. On the second hospital day the blood sulfanilamide level was 11.7 mg. per 100 cc. The blood showed a white-cell count of 34,000. She had a well-marked anemia. During the night she had another chill lasting a half hour followed by a temperature of 104°F. A transfusion was given in the afternoon. On the fourth hospital day she had a second transfusion during which she had a severe chill, the

temperature going to 105.6°F. During the night the temperature dropped to normal, where it remained. She was prostrated but had no complaints and no abnormal physical signs. The next day she had oliguria despite a fluid intake of 3000 cc. Sulfanilamide therapy was stopped, the blood level being 14 mg. per 100 cc. Her blood pressure was 95 systolic, 60 diastolic. There were several loose stools. She had become nauseated. The nonprotein nitrogen of the blood serum was 142 mg. per 100 cc. On the following day her blood pressure was 95 systolic, 60 diastolic, becoming 105 systolic, 50 diastolic after two doses of coramine by mouth. She continued passing only small amounts of urine of a low specific gravity. Her temperature was normal. On the tenth hospital day she remained drowsy and vomited small amounts. At this time she was quite jaundiced. Her urinary output had risen to 64 ounces. She refused to take anything by mouth. The area of liver dullness was not diminished, nor was there any tenderness in the abdomen. The chest remained clear and the blood pressure steady at 105 systolic, 50 diastolic. Her sulfanilamide blood level was 9 mg. per 100 cc., nonprotein nitrogen 137 mg. per 100 cc., chlorides 446 (as sodium chloride), icteric index 50 to 60. The red-blood-cell count was 2,600,000, the white-blood-cell count 25,500. The smear was not remarkable. She continued rapidly downhill. On the fourteenth hospital day her stomach seemed to be distended and an unsuccessful attempt was made to pass a nasal tube. She rapidly failed and died on the fourteenth hospital day.

Differential Diagnosis

Dr. Wyman Richardson: I feel badly about the statement, "well-marked anemia." I do not know whether she looked anemic or not, or whether anyone did the blood count. This is somewhat important, as you will see later on. However, we will take that as it is written.

We have to explain in this patient fever and chills, evidence of renal failure, jaundice, anemia and death. I want to take them up in that order. In the first place, in regard to her sepsis, we have no report anywhere in the record of a blood culture or a throat culture. The clinical description of her disease is typical of beta-hemolytic streptococcal throat infection which has been so prevalent in the past few months. The whole story down to her admission to the hospital is one of a hemolytic streptococcal throat infection. The question is, Do we have to go any farther than that in regard to her sepsis? They have ruled out the possibility of a meningitis fairly well by the lumbar puncture. There is nothing in the story to suggest any localizing lesion except the renal failure and the jaundice, with the possible exception of the to-and-fro scratching sound over the pulmonic area. This, from the description, was more likely some sort of pleuropericardial rub and of no significance. However, we cannot dismiss entirely the possibility that this patient might have had acute bacterial endocarditis to account for some of the sepsis.

In regard to the question of renal failure, she had oliguria and a rapidly rising nonprotein nitrogen with, at the same time, a blood pressure which remained low. Little is said about the organized sediment in the urine, which might have been of help. In bacterial endocarditis we frequently have a nephritis which is usually embolic in, I think, 90 per cent of cases, but it may be a true glomerulonephritis in the remaining ten per cent. However, in this case it is very difficult for me to see how the patient would reach this rapid termination in so short a time. Most of them will go on longer. Certainly if it were a focal nephritis from streptococcal infection, again the course would not be so fulminating. I would not expect even acute glomerulonephritis to go to this point so quickly. Nothing is said about hemorrhage from the kidney. It is mainly a matter of anuria for a good many days. I note, however, that her urinary output did increase shortly before death.

Let us leave the discussion of renal failure for a moment and go on to the symptom of jaundice. She had a large amount of sulfanilamide which was trapped in the blood stream when the kidneys shut down and remained there for six or seven days. She is entitled to have a hemolytic type of anemia from sulfanilamide. In such a case one would expect to find in the blood smear more evidence of red-cell regeneration, although it is possible that sepsis may inhibit the bone-marrow response. The cases of hemolytic anemia from sulfanilamide that I have seen have shown obvious evidence of red-cell regeneration on examination of the smear. However, if she did have hemolytic anemia from sulfanilamide she is entitled to a small amount of icterus but not an icteric index of 50 or 60, if we can take that as accurate.

Another thing we have to consider is toxic hepatitis on the basis of either infection or sulfanilamide. I do not know of any case of real toxic hepatitis as a result of sulfanilamide, but I am sure that we are going to see them and it may be that this is one. I note that, when patients get too large doses of sulfanilamide for a long time, their breath begins to have a sweetish, musty odor. This to me indicates liver failure and it is always a warning to stop sulfanilamide at once.

The question whether this anemia might be due to the sepsis alone is impossible to determine.

It might be due either to sulfanilamide alone or to sepsis or most probably to both. In regard to one laboratory finding, the low chloride, the exact explanation is not clear, although it may have been the result of the previous high fever and sweating with considerable vomiting. I should think that was the most reasonable explanation.

She died, and why did she die? I think as you look over this story you find that things were progressing quite well when she had an episode of leukopenia which scared her physician. He stopped the sulfanilamide and the patient responded rapidly. She was still septic, however, as many of the patients with streptococcal disease have been this year. Then something happened. On the fourth hospital day she was given a transfusion during which she had a severe chill. She has had so many chills that we may have become more or less desensitized to them. She has a transfusion, a sudden chill, and oliguria. I believe this patient was given incompatible blood; and that she had agglutinins in the blood serum of low titer, so that immediate reaction was not apparent; but that she did have transfusion renal failure. If that is the case it might cause hemolysis of the donor's cells and increase the icterus to a slight extent but not to 50 or 60. I still do not think we have explained her severe jaundice. I think the severe jaundice is due to what Dr. Mallory will call a toxic hepatitis, which I believe is due to sulfanilamide, but it may not be possible to tell whether it is that or toxic hepatitis from infection. I should like to say one thing more. I may be wrong about the transfusion reaction. It is said to be due to plugging in the kidney tubules, due to precipitation of hemoglobin. That may be true and is a perfectly good theory. I would ask why the patients with paroxysmal hemoglobinuria have hemolysis of the blood, often massive, and still do not go into immediate renal failure. I do not see any difference, although there may be some explanation I do not know about. It is of course conceivable that there is some infectious process in the abdomen, an appendix with appendiceal abscess or phlebitis and multiple liver abscesses, jaundice and death. I mention them but I see no evidence for them, and I will not consider them further. I will say, then, that the patient had infection with beta-hemolytic streptococcus, arising in the throat, that she had an incompatible transfusion, with renal failure, and that she had a toxic hepatitis on the basis of prolonged administration of sulfanilamide.

Dr. Tracy B. Mallory: Are there any suggestions?

Dr. William B. Breed: Would you on examination be able to determine that a patient had died as a result of incompatible transfusion?

Dr. Mallory: I believe so.

Dr. Breed: On what basis?

Dr. Mallory: I shall proceed to tell you because I think that was the case here.

Clinical Diagnoses

Acute yellow atrophy of liver.
Sulfanilamide poisoning?

Dr. Richardson's Diagnoses

Beta-hemolytic-streptococcal infection (arising in throat).
Incompatible transfusion, with renal failure.
Toxic hepatitis.

Anatomical Diagnoses

Sepsis, type undetermined.
Septic infarction of the lung with abscess formation.
Hemoglobin nephrosis.
Toxic hepatitis, slight.

Pathological Discussion

Dr. Mallory: As you have noted from the record this patient was never in the Massachusetts General Hospital, although she was seen by various members of our staff in consultation. At autopsy the kidneys were a little enlarged. They weighed 400 gm. whereas 300 gm. would have been a fair size for a woman of her build. The gross characteristics were not very striking. There were some reddish spots that looked hemorrhagic, but the cortex was only slightly swollen. On microscopic examination the outstanding feature was the plugging of most of the collecting tubules with orange masses of precipitated hemoglobin. It is, I think, difficult when looking at sections from a case of this sort to convince oneself that every tubule is plugged and that the renal insufficiency can be explained purely by intranephritic hydronephrosis as has been claimed.

There is a certain amount of experimental work* which is interesting in this regard. It has proved possible in dogs to produce renal shutdown by hemolytic agents or the infusion of hemoglobin in solution, and it has been found that the development or the failure of development of renal insufficiency apparently depends on the reaction of the urine. If the urine is acid at the time that the hemoglobin passes through the glomerulus it is apparently precipitated in large amounts in the tubules. If the animal has previously been given alkalies in sufficient quantity to keep the urine alkaline no renal deficiency develops. The ex-

*DeGowin, E. L.; Warner, E. D., and Randall, W. L.: Renal insufficiency from blood transfusion. II. Anatomic changes in man compared with those in dogs with experimental hemoglobinuria. Arch. Int. Med. 61:609-630, 1938.

perimental results seem clear cut and seem to check very closely with the formation of the hemoglobin casts, so that at the present time it seems reasonable to me to accept the theory.

In addition to the kidney findings there was a septic tonsillitis. There had evidently been some degree of thrombophlebitis in the peritonsillar veins because the lungs showed multiple septic emboli and the beginning of abscesses. There was no endocarditis and there was neither pleuritis nor pericarditis to explain the rub.

Dr. Champ Lyons: The course of this disease strikes me as being more like that caused by the staphylococcus than the streptococcus. Were there any cultures?

Dr. Hugh A. Stout: The postmortem blood culture was sterile.

Dr. Mallory: The liver showed jaundice. It was swollen and there were a few more leukocytes in the sinusoids than normal, certainly no extensive destruction of liver cells. I think one can say that there is a minimal hepatitis; whether it was due to the transfusion reaction, to the sepsis or to sulfanilamide, I certainly cannot say. There was no extensive hepatitis, however.

Dr. Richardson: One is at a loss to explain the jaundice. If this were *Staphylococcus aureus* septicemia there might be a hemolytic anemia, increasing the jaundice that you get from sulfanilamide.

Dr. Bernard M. Jacobson: I should like to ask if sulfanilamide renders typing of the blood at all difficult.

Dr. F. T. Hunter: It should not interfere if the typing is properly carried out.

Dr. Breed: I should like to ask why it seems more like a staphylococcal than a streptococcal process.

Dr. Lyons: There are several things that made me think of that. First, she had an abrupt onset of chills with a fever that did not respond to sulfanilamide therapy. The white count went to 3400 on administration of sulfanilamide, but it did not similarly drop on the second administration of comparable doses. I think leukopenia is more apt to be associated with staphylococcal infection because of the leukocidin toxemia. The late recurrence of chills again is suggestive of a septic thrombophlebitis and the late thrombophlebitis with the manifestation of chills is much more apt to go with staphylococcal than streptococcal infection because of the nature of the inflammatory response that is elicited by staphylococcus. I think that the jaundice and the miliary lung abscesses which progressed after the acute infection subsided are more suggestive of staphylococcus than streptococcus when one considers the amount of sulfanilamide that was given.

A Physician: Is sulfanilamide as apt to render the blood culture negative in staphylococcal infections as in streptococcal ones?

Dr. Mallory: I should think not.

Dr. Edward A. Gall: What is the opinion regarding the height of jaundice following incompatible transfusion?

Dr. Hunter: That is hard to know because she had hemoglobin with much brownish color so that the icteric index is often read three times as high as it should be. A van den Bergh reading would be better.

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THE SCIENTIFIC AND COMMERCIAL EXHIBITS AT THE ANNUAL MEETING

THE forthcoming meeting of the Massachusetts Medical Society is featuring twenty-one scientific exhibits. The Massachusetts Department of Public Health will demonstrate not only several different types of work directed from the State House but also that carried on at the Rutland State Sanatorium and the Pondville Hospital. Certain important activities of the American Medical Association, such as the dissemination of information concerning syphilis, the work of the Council on Foods, the Council on Physical Therapy and the Council on Pharmacy and Chemistry, will be shown in a series of booths.

In line with the policy of the Committee of Arrangements to stimulate interest among the local hospitals to exhibit certain of their activities and interests, there will be four exhibits by members of the staffs of the Worcester hospitals. These include demonstrations of pathologic lesions in the genitourinary tract and of the treatment of certain types of fractures. An unusual exhibit on the production of milk with a high mineral content is to be put on by the medical milk commissions of Boston, Worcester and Springfield. This is the first time that a demonstration of this type has been shown in the Scientific Exhibits, and all physicians should become acquainted with the modern methods of improving the quality of one of our basic foods.

So much is offered in these scientific exhibits that is of interest and value to practicing physicians that none should fail to avail themselves of the opportunity to learn about some of the recent advances in medicine.

The number of commercial exhibits at this year's annual meeting is greater than ever before. Many old friends are back, and in addition, a number of well-known medical-supply houses are exhibiting for the first time. It is hoped that, old or new, they will be received with a keen show of interest. It should be realized that it is the amount of interest shown by physicians as evidenced by their visits to the various booths, that in the end determines the amount of exhibition space sold at these meetings, and hence their cost to the Society.

Many of these exhibits are extremely interesting and have been designed to show in an attractive form the new products as well as time-tested ones. Much can be learned, if the physician is willing to spend a little time in examining them. Everyone is urged to register at all the commercial exhibits, and thus help to ensure prosperous meetings in the future.

THE LITERARY PHYSICIAN

FEW physicians have led a more harassed life than Tobias Smollett. Overwhelmed with his editorial duties with "his minions about him, to whom he prescribed tasks of translation, compilation or abridgement,"[1] three months in jail and the death of his daughter, Betty, in 1763, brought him to the breaking point. In June, 1763, he crossed the

Channel for a protracted tour to Paris, Lyons, Montpellier and finally the Riviera, making his headquarters at Nice from November, 1763, to May, 1765. He shrewdly saw the great future of Nice and Cannes and envisaged the Cornice road, later designed by Napoleon. Although of choleric temperament and somewhat jaundiced in most of his views of what he saw abroad, he nevertheless had his letters published on returning to London in 1766. These *Travels through France and Italy* (London, 1766) give an accurate account of what he observed and served to stimulate interest in the Riviera as a pleasure and health resort.

There is little of medical interest in the two volumes, although some of the letters are to a doctor. In Montpellier he consulted a celebrated French professor of medicine by a letter written in Latin. The reply, in French, indicates that the learned gentleman could not read Latin or did not bother to read Smollett's notes. When sent back, with passages marked, the answer was equally irrelevant. Guessing the cause of Smollett's illness to be tuberculosis, he advised turtle-soup! Smollett was not well. His asthma and rheumatism prevented him from looking up some manuscripts for his friend, John Hunter. In Nice he kept a detailed register of the weather from November, 1763, to March, 1765, which is appended to his *Travels*.

Smollett's whole life, however, is of more than usual interest to physicians. After an apprenticeship of five years with a doctor, Smollett became a fleet surgeon and later lived in Jamaica, where he married his Creole wife, who was so devoted to him in his latter years. Returning to London, he was closely associated with Hunter, Pitcairne and Smellie, while practicing surgery. He was soon drawn to coffee-house society, became noted as a raconteur and, in spite of a move from Westminster to Mayfair to gain practice, the world of letters was more to his liking. *Roderick Random* came early, published when he was only twenty-seven; *Peregrine Pickle* and *Count Fathom*, a few years later. *Humphrey Clinker*, his masterpiece, was written in 1770, in Italy. His life was drawing to a close and he wrote John Hunter in 1771: "If I can prevail upon my wife to execute my last will, you shall receive my poor carcass in a box after I am dead to be placed among your rarities. I am already so dry and emaciated that I may pass for an Egyptian mummy without any other preparation than some pitch and painted linen."[2] Dying in Italy, however, he was buried two days later in Leghorn; his wife, apparently, thought that best.

REFERENCES

1. Seccombe, T.: Tobias George Smollett (1721-1771). *The Dictionary of National Biography*. Vol. 18. New York: The Macmillan Co., 1909. P. 586.
2. *Ibid.*: P. 588.

MASSACHUSETTS MEDICAL SOCIETY

ANNUAL MEETING NEWS

Moving Pictures

The value of moving pictures in the demonstration of medical topics is well recognized. This year the Committee of Arrangements has procured a large number of films illustrating a variety of conditions, and has arranged to present these as a continuous program from 10 a. m. to 5 p. m. on Tuesday and Wednesday, June 6 and 7. These pictures will be shown in the Musicians' Room, which is on the main floor of the Municipal Auditorium. The program will be run on a published schedule and consists chiefly of fifteen-minute films. This arrangement will make it possible for members to select the topics of individual interest at convenient hours. Mr. Warren Sturgis, who is specializing in the production of medical moving pictures, will be in direct charge of the program. On Thursday morning, an opportunity will be given for repeating those films in which the greatest interest has been shown during the two preceding days.

GOLF TOURNAMENT

The Golf Tournament, which has become so much a part of the June meetings of the Society will be held at the beautiful Wachusett Golf Club in West Boylston, a four-mile drive from the Auditorium. An innovation will be made this year in that play will be possible on two afternoons instead of one as has formerly been the case. This change has been made so that golfers can arrange their program and not miss meetings in which they are particularly interested. The starting play on the afternoons of Tuesday and Wednesday, June 6 and 7, will be from 1:30 to 3:00 o'clock, and the greens fees will be $1.00 on Tuesday and $1.50 on Wednesday.

The principal prize this year, as last, will be

the honor of having one's name inscribed on the Burrage Bowl, presented last year by Dr. Walter S. Burrage in memory of his father the late Dr. Walter L. Burrage, who was secretary of the Society for so many years. Custody of the bowl, which is awarded for the low net score, was won last year by Dr. Roy E. Mabrey. The local committee in charge of the tournament is offering prizes for the three low net scores and the three low gross scores and three for the winners in the kicker's tournament. Club or state handicaps will be necessary in playing for the net or gross prizes.

The prize winners this year will have the distinction of receiving their prizes at the annual dinner where the presentations will be made by the president, Dr. Channing Frothingham. A luncheon will be served to any members who wish to eat at the club before starting play. Reservations can be made by telephoning the club at West Boylston 110.

At the registration desk in the Auditorium there will be handbills giving directions to reach the club and any other necessary information.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

BLEEDING IN THE PUERPERIUM

Mrs. M. G. M., a thirty-year-old gravida II, was discharged from the hospital on the eighteenth day following a normal delivery and convalescence. On January 13, 1936, two days after she arrived home, she reported by telephone that she was flowing very freely.

The family history was non-contributory. The patient had had scarlet fever and measles in her childhood. She had had a routine tonsillectomy but no other operations. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted seven days, with no discomfort. Her last period was March 13, 1935, making the estimated date of delivery December 18. Her first pregnancy had been terminated by a simple forceps delivery after a labor of not over six hours.

As she lived 20 miles in the country, a physician in a nearby town was asked to see her following the telephone call. Three quarters of an hour later the bleeding recurred, and it was advised that she be brought into the hospital. There was a great delay in getting an ambulance, and the patient did not arrive at the hospital until three hours after she had first been seen. On entry she was pulseless, no blood pressure could be obtained, and she was still flowing, but not excessively. One-quarter grain of morphine was given immediately, and under nitrous oxide and oxygen anesthesia a vaginal examination was performed. A large piece of retained placenta was found in the cervical canal. This was removed by the fingers, and an iodine strip was left in the uterus. Intravenous glucose solution was given at the start of the operation. Half an hour later the blood pressure was 60 systolic, 40 diastolic, and after another half hour 90 systolic, 60 diastolic. The pulse at the latter time was definitely palpable, with a rate of 110. It was believed that, although the need of transfusion was not urgent, convalescence would be improved if it were done. In consequence, a citrate transfusion of 750 cc. was given, the husband of the patient being used as the donor. The pack was removed from the uterus the day following operation, and there was no subsequent bleeding. For several days her temperature ranged from 100 to 101°F. in the afternoon. She was discharged from the hospital two weeks after entrance.

The following is a report of her blood examinations: January 14, hemoglobin 50 per cent, red-blood-cell count 2,270,000; January 18, hemoglobin 60 per cent, red-blood-cell count 2,820,000; January 21, hemoglobin 70 per cent, red-blood-cell count 3,070,000; January 27, the day of discharge, hemoglobin 75 per cent, red-blood-cell count 3,820,000.

Comment. The retention of a piece of placenta is the commonest cause of serious bleeding in the puerperium. In this particular case the placenta was looked at carefully when the baby was born, and although it was a little irregular, it was not evident that a piece remained in the uterus. Even if it had been thought that a piece of it had been left, conservatism would have been the ideal treatment in the absence of any undue bleeding during the entire stay in the hospital.

This hemorrhage came on very suddenly and without warning, and the patient must have flowed tremendously. It was unfortunate that the delay occurred in getting her into the hospital. When she arrived, she was in very poor condition. Transfusion was not done immediately because there was still some bleeding and it seemed very important that this be stopped.

It cannot be advised too strongly that all cases of bleeding should be checked by blood examination; only in this way can the total amount of blood loss be accurately determined — observation gives only an estimate at best. Furthermore, the therapeutic value of transfusion cannot be overemphasized.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

LEGISLATIVE NOTES

At a meeting of the Committee on State and National Legislation, on Wednesday, May 24, the Chairman was authorized to go before the Senate subcommittee considering the Wagner Bill. The final wording of his statement was arrived at only after consultation with Senators Lodge and Walsh and after a detailed discussion of it with Drs. Edward H. Cary, Walter F. Donaldson, Roscoe L. Sensenick, Olin West, Morris Fishbein, William C. Woodward, and William D. Cutter of the American Medical Association who helped to bring it into its final form and unanimously approved it. Dr. Cary, who presided over the Association opposition to the bill, introduced the writer to the subcommittee.

STATEMENT OF DR. CHARLES C. LUND, OF BOSTON, MASSACHUSETTS, CHAIRMAN, COMMITTEE ON STATE AND NATIONAL LEGISLATION OF THE MASSACHUSETTS MEDICAL SOCIETY, TO THE SUBCOMMITTEE OF THE COMMITTEE ON EDUCATION AND LABOR OF THE UNITED STATES SENATE, CONSIDERING THE WAGNER BILL, SENATE 1620, MAY 26, 1939

The Council of the Massachusetts Medical Society, which is our legislative body, has not met to consider the Wagner Health Bill, Senate 1620. However, the Committee on State and National Legislation has given the bill very serious consideration and has authorized my appearance to discuss it.

At the present time the United States Government in one way or another is carrying on or aiding medical activities through a great multitude of bureaus and departments. These activities operate under a great mass of diverse laws and regulations and are not always well co-ordinated. President Roosevelt has, with the consent of Congress, just taken a step of fundamental importance that has met with widespread approbation even in New England. That step is the regrouping of several agencies of the government. Is it too much to expect that the majority of the present federal medical activities (except the Army and Navy services), and all future ones, if new ones are created, shall be placed together? We realize that there were probably sound reasons to explain how the present complex situation arose. But is such a situation still sound? The greatest defect in the bill is that it not only perpetuates overlapping of medical activities in separate departments but even adds to overlapping by giving the Social Security Board new and widespread medical functions.

How cumbersome this proposed situation is may be seen by the authorization in the bill of 245 and more state and federal advisory councils (not counting those for the District of Columbia, and so forth). Now the advisory council idea is, per se, excellent. But there should be one federal council and one council for each state and territory, —not five for each. Also, these councils should be created at once and given the broadest possible advisory powers, so that they would have under their consideration any medical problems arising in connection with any governmental activity. The councils should be so constituted that the medical profession and the public are both adequately represented. Our state health department is well run by such a council.

The provision in the bill that gives the Federal Government the power to refuse grants to states that do not have a merit system of appointment and promotion in the departments spending the grants is, in our mind, very good and one of the most important provisions of the bill. Of course, we don't want any more interference in our local affairs than is necessary. But we feel that we have a right to be assured that any federal funds spent on the care of the needy will not pass through the hands of inefficient political appointees.

In this connection, we have another suggestion. One item in the cost of illness is the cost of medical care of totally needless illness. We in Massachusetts naturally object to paying for the care of such patients either in our own or any other state. It would not require any federal funds for every state to abolish smallpox. The methods of doing this have been available for years. The cost is low and well within the possibilities of budgeting by the poorest states. Nevertheless, why was the average incidence of smallpox in this country 7600 cases per year from 1933 to 1937, inclusive? Purely because the responsible officials and the public have either failed to see that the proper control laws have been passed by their legislatures or they have not enforced their laws. We suspect that either the educational, political, or public-health organization in these states is of such a nature that subsidized medical care might not be appreciated or efficiently utilized.

TABLE 1. *Cases of Smallpox During the Five-Year Period (1933–1937, Inclusive) and Annual Rate per 100,000 Population by Type of Vaccination Laws.*

STATES WITH COMPULSORY VACCINATION	CASES	RATE	STATES WITH LOCAL OPTION	CASES	RATE	STATES WITHOUT COMPULSION	CASES	RATE
Massachusetts	0	0	Maine	0	0	Delaware	1	0.08
Pennsylvania	0	0	New Jersey	0	0	Vermont	3	0.16
Rhode Island	0	0	Florida	25	0.3	Michigan	298	1.26
Maryland	1	0.02	Connecticut	29	0.35	Arizona	40	1.96
New Hampshire	2	0.08	No. Carolina	109	0.64	Oklahoma	512	4.08
Dist. of Columbia	4	0.14	Georgia	119	0.78	Illinois	1773	4.54
New York	189	0.30	Tennessee	168	1.18	Nevada	29	5.86
Virginia	61	0.46	Ohio	467	1.40	Indiana	1022	5.96
So. Carolina	84	0.92	Alabama	211	1.48	California	2402	8.02
Kentucky	154	1.08	Mississippi	166	1.66	Utah	260	10.10
West Virginia	110	1.22	Louisiana	212	2.00	Minnesota	1729	13.14
Arkansas	482	4.82	Texas	2515	8.28	Missouri	2585	13.22
New Mexico	103	4.88	Colorado	973	18.28	Wisconsin	2828	19.42
			Oregon	1466	29.08	Kansas	2126	22.64
						Iowa	3162	24.96
						No. Dakota	1096	31.32
						Washington	3029	37.10
						Nebraska	2583	37.88
						So. Dakota	1515	43.78
						Idaho	1076	44.92
						Wyoming	796	68.62
						Montana	2467	92.92
Totals	1190	—		6460	—		31332	—
Cases per year	238	0.57		1292	3.43		6266	14.1

Now we want to discuss a purely financial question that we know is uppermost in the minds of many doctors who criticize this bill vociferously. That is, where is the money coming from to pay the bills? Only a few doctors start to practice medicine with any capital except what they have invested in their education. They expect to save money and invest it for their old age, if they can. The immediate effect of this bill would probably be to increase the incomes of some doctors. That, of course, would be of immediate benefit for them. But doctors are trained to look beyond immediate results in all their work. Here they look at a government that has been going "into the red" for many years. They realize that much of the increase in debt was not to be avoided. In so far as the enactment of this bill may increase the expense of government, it will further the tendency to inflation that many people think is steadily in progress. The doctors wonder, and in this they are like millions of other Americans, what their savings will be worth some years from now. The doctors

would look with more favor on a bill that went much more slowly and which did not contain in any place the rather frightening phrase "such sums as may be needed to carry out the purposes of this title," coming as it does repeatedly, after the mention of sums, which, while they may not be very large in the national economy, seem enormous to the individual citizen.

There are wide discrepancies among various estimates that have been made as to the number of people who for financial reasons now do not obtain medical care. Everyone admits that the group that most needs to be provided with medical care is that group which has no appreciable income on which to exist. We suggest that before starting to furnish federal aid for the medical care of employed people, medical care to be furnished under the bill be limited to the indigent and the medically needy. If the lowest estimate of the numbers of medically needy and indigent persons is correct it will be a very small matter to rectify — but, if the highest estimate is correct, the problem is so enormous that it will take all the possible available resources in money and trained men, without at the same time taking on the other even greater problem of aiding in the care of those who are better off.

I make a plea for co-operation between the doctors and the government. In Massachusetts a most remarkable thing has happened. The adjusted death rate for cancer in women has been decreasing for five years and the rate for men has become level. This is the only state in the Union where this has occurred, and it has not occurred in any foreign country. This has been accomplished by the simultaneous use of two means. First, the establishment of state-aided cancer clinics about twelve years ago helped a little. But during the first few years of operation of the clinics there was no decrease in the elapsed time from the onset of the cancer to first treatment of it which is the most important factor in controlling an individual case.

Secondly, for five years, the State Department of Health has been promoting the education of the public in an original manner. Women's clubs are stimulated to ask for lecturers on cancer. They are encouraged not to go outside their town in search of an expert, but to invite one of their general practitioners. If the doctor believes that he is not prepared to give such a talk, he is provided with suitable material prepared for him by the Massachusetts Medical Society and the State Department of Public Health. This serves two purposes: (1) it educates the public, and (2) it educates the doctor. The cases are now coming in months earlier and the results improving steadily.

SUMMARY

If federal legislation concerned with the public health is to be enacted, it should be directed toward the following objectives:

1. Unification of most of the present medical services of the federal government, except the Army and Navy services. All future federal medical activities should be added to this group.

2. Representative medical advisory councils to work with the federal and state medical officers.

3. Expansion of activities where clear evidence of need for expansion is proved.

4. Support of existing recognized hospitals, rather than building new governmental ones for the care of the indigent, thus reducing the number of vacant hospital beds instead of increasing it.

DEATHS

HOLTON — Charles E. Holton, M.D., of 391 High Street, Medford, died May 22. He was in his seventy-second year. Born in Lee he received his degree from the University of Vermont College of Medicine in 1892. For more than thirty years he was an investigator in the food and drug control division of the United States Department of Agriculture.

Dr. Holton was a former member of the Massachusetts Medical Society.

His widow and a daughter survive him.

MAYO — Charles H. Mayo, M.D., of Rochester, Minnesota, died May 26. He was in his seventy-fourth year.

Born in Rochester, Minnesota, he received his degree from Northwestern University Medical School in 1888. With the death of his father, he and his brother inherited a general practice and their father's interest in St. Mary's Hospital. The Mayo Clinic was formally organized in 1912, and in 1915 the Mayo brothers gave $1,500,000 to establish the Mayo Foundation for Medical Education and Research in affiliation with the University of Minnesota. Dr. Mayo was a past-president of the American Medical Association and the American College of Surgeons.

Among his affiliations were fellowships in the American Medical Association, American Surgical Association, Southern Surgical Association, Western Surgical Association, American College of Surgeons and the Society of Clinical Surgery. He was professor-emeritus of surgery at the University of Minnesota Medical School.

His widow, a son, Dr. Charles W. Mayo, four daughters, and a brother, Dr. William J. Mayo, survive him.

SHINN — Philip A. Shinn, M.D., of Rockland, died May 23. He was in his fifty-fifth year.

Born in Portland, Maine, he received his degree from Tufts College Medical School in 1915, and interned for two years at the Robert Breck Brigham Hospital, Boston. Dr. Shinn was a lieutenant in the naval medical corps during the World War and served more than a decade at the veterans' hospitals in Northampton, and Augusta, Maine. Eight years ago he joined the staff of the Boston Dispensary.

He was a member of the Massachusetts Medical Society, the American Medical Association, the American Psychiatric Association and the New England Society of Psychiatry.

A son and a daughter survive him.

MISCELLANY

MAINE NEWS

Report of the Cancer Committee

A review of the activities of the Cancer Committee reveals evidence of individual and collective co-operation rather than separate endeavor of the committee as a functioning unit. In other words, the work of the members of the committee has been so closely tied up with the public activities of the Women's Field Army for the Control of Cancer that there has been little room for other projects by the former. However, it would seem that this particular method of presenting constructive cancer work has not been without evidence of progress.

The educational campaign of the Women's Field Army has been eminently successful. To this campaign, various members of the Cancer Committee have contributed much in personal time and effort. Speaking before lay groups

and by radio, the medical aspects of cancer have been frequently presented. Positive results of this campaign have been noted in the steadily increasing number of individuals who have visited the tumor clinics for advice and treatment. No new tumor clinics have been added during the past year. The list is as follows:

Central Maine General Hospital, Lewiston; Eastern Maine General Hospital, Bangor; Maine General Hospital, Portland; Sisters Hospital, Waterville; St. Mary's General Hospital, Lewiston; Thayer Hospital, Waterville.

Members of the Cancer Committee have served as clinic personnel, along with other members of the institutional staffs.

Figures from the office of the Women's Field Army show that the Joseph W. Scannell Memorial Fund was exhausted October, 1938, so great was the increase in demand for services to the indigent. Benefits from this fund were widely distributed throughout the State.

The question has been brought up of placing other diagnostic clinics at strategic points in the State in areas not now easily covered. These would serve to lighten the load on some of the large centers. A study of this problem is now going on, and key men are being contacted with the idea of inaugurating such diagnostic centers. Because of the requirements of high-voltage roentgen therapy and radium, only the large clinics are likely to carry on the therapeutic measures of radiation.

Early in the year a symposium on cancer was prepared by a committee member, Dr. Edward H. Risley, of Waterville, acting also in his capacity as chairman of the Advisory Board of the Women's Field Army. Contributions to this symposium were made by members of the Cancer Committee and other medical members of the Advisory Board. Under appointment, requested by the Committee on Graduate Education, Dr. Risley plans to offer this symposium for panel presentation at a meeting of the county medical societies.

In review it may be stated that cancer work in the State is much more active than it has been for years. The educational activities of the Women's Field Army for the Control of Cancer, backed by the personal and professional co-operation of the members of the Maine Medical Association, are helping the laity, as a whole, to become more and more cancer-conscious. The biggest problem now seems to be to synchronize the educational work with funds available for carrying the increasing load of indigent patients who seek treatment for cancer.

FORREST AMES, *Chairman.*

REPORT OF COMMITTEE ON GRADUATE EDUCATION

One of the most important responsibilities facing state medical associations is that of providing an adequate program of graduate education. The problem varies in different states, due to many local factors. Consequently there are bound to be many variations among the several programs which are being developed. A permanent organization of the different state committees on graduate education has been effected, for mutual benefit and exchange of ideas. Your chairman has attended each meeting of this central organization and plans to be present at the next meeting in St. Louis at the time of the meeting of the American Medical Association.

Your committee has had several meetings during the year and has been in conference with the Council and the county secretaries.

Because of the unique advantage accruing to the State through the Bingham and the Commonwealth fellowships, our program naturally becomes divided into two parts: the first is intramural and is concerned with making available adequate educational programs within the State; and the other has to do with the wider utilization of courses available in Boston.

It was decided to develop our intramural program in conjunction with the county societies. After some experimentation, in an endeavor to find the most interesting type of program, a series of panel discussions were prepared and offered to the county societies. Panels on the following subjects are now available: "Pneumonia," "Cardiovascular Disease," "Fractures," "Acute Appendicitis and Complications," "Laboratory Methods and Their Application in Clinical Medicine," "Surgery of the Thorax" and "Cancer." It is expected that panels concerning other subjects will be developed from time to time, depending on the demand. So far this type of program has seemed very popular and worthwhile.

Your committee has co-operated with the directors of both the Bingham and the Commonwealth funds in an endeavor to have the available fellowships allocated where they are most needed. For the most part these fellowships have been intended for men practicing in the small communities. As nearly as can be estimated about 15 per cent of our members have taken advantage of these fellowships. Perhaps another 10 per cent have been providing their own educational programs through long-established hospital or society affiliations — and need not enter the picture. Of the remaining 75 per cent, eliminating the men near retirement age, there must be about 50 per cent who should have facilities for some form of graduate study. An intramural program is essential in order to reach them. In turn, this may stimulate interest in some phase of our extramural program. At present it does not seem necessary to expand our program but rather to co-ordinate and develop what we already have. The sole exception to this might be where, in certain counties, such as Aroostook, the geographical problem makes it difficult to attend meetings, especially during the winter. Here it might be well to consider the question of intensive intramural courses — to be given during the summer. If there be sufficient local interest, such a program can be developed and financed without expense to the local groups. It is understood that the Bingham Associates are developing another form of fellowship, giving short intensive courses of one week's duration. These will provide study on more specialized subjects than heretofore available and should appeal to a greater number of our members.

The following recommendations are made:

(1) Greater co-ordination between the programs of the annual meeting and the Fall clinical session and the program of graduate education. While there is no desire to interfere with the committees in charge of these two annual events, the Committee on Graduate Education necessarily must have a long-range viewpoint, and co-operation between these committees might result advantageously for all concerned.

(2) Continuation of the panel-discussion type of program — through the county societies.

(3) Further development of the hospital-staff program, utilizing the available material for case study.

(4) Participation of the association as an organization in the New England Postgraduate Assembly. This has already proved its usefulness. It offers a great deal in the way of postgraduate education.

(5) Co-operation with the Bingham and the Commonwealth funds in the extramural programs — through greater utilization of the available fellowships. Through application to the committee, courses on any desired subjects may be obtained for groups of four men.

F. T. HILL, *Chairman.*

Report of the Advisory Committee on Syphilis Control

The committee presents the following reports received from Dr. Roscoe L. Mitchell, assistant director of the State of Maine Department of Health and Welfare.

During the year the director of the division gave thirty-six lectures mostly to lay persons on the subject of venereal disease, the total attendance being about 3300 persons. About 800 pieces of educational literature were sent out in response to requests.

The Diagnostic Laboratory performed 19,080 Kahn tests and 17,658 Hinton tests. Examinations for the presence of gonococci totaled 5827, 162 of these being performed at the branch laboratory in Caribou.

No record is available of the number of syphilis treatments given by private physicians. The Bureau of Health receives reports from the twenty-seven state clinics, and their totals for the year 1938 were 11,846 doses of arsenicals and 12,948 doses of heavy metals.

During 1938, 58 per cent of the newly reported syphilitic patients were attending the clinics, whereas 60 per cent of the new cases of gonorrhea were being treated by private physicians.

Case reports give a total for 1938 of 588 cases of gonorrhea, 487 being acute, 90 chronic and 11 not stated. Five hundred and seventy-two cases of syphilis were reported, the stages being as follows: 95 primary, 139 secondary, 289 tertiary, 36 congenital, 8 latent and 5 not stated.

Free drugs of all sorts were issued by the bureau to 130 physicians, exclusive of the material furnished to the state clinics.

Maine Medical Legislation in 1939

L.D. 873. Hospitals must admit osteopaths to practice in them and must do all laboratory work required by osteopaths. Not passed.

L.D. 22. Dr. Pratt's amendment to the Medical Examiners' Bill. Passed in the last week of the session after a very stormy career. Essential changes: number reduced to two each in the counties of Franklin, Hancock, Knox, Lincoln, Piscataquis, Somerset, Sagadahoc and Waldo; three each in Oxford and Washington; four each in Aroostook, Kennebec and York; five each in Androscoggin; six each in Cumberland and Penobscot. The Governor may appoint as many more as he considers advisable; not passed. The law will not take effect until January 1, 1941, that is, after the present Governor retires from office; consequently, the present Governor will not be embarrassed by failure to reappoint.

L.D. 581. Sale of opium derivatives only on prescription. Passed.

L.D. 472. Sale of barbituric acid derivatives or compounds only on prescription, except for personal administration by a doctor, dentist or veterinary to his own patients. Passed.

L.D. 820. Dispensation of marijuana forbidden. Not passed.

L.D. 874. Hospitals (and inferentially others) may charge only $3.00 for x-ray pictures. Not passed.

L.D. 880. United States uniform narcotic law. Not passed.

L.D. 471. Requiring pre-marital examination for venereal diseases. Amended to require merely a prenatal examination. Requires every physician to take during gestation a blood sample and submit it to the State Laboratory. Passed in this amended form during the last week of the session. Recalled from the Governor's office and had the words added, "and no civil action shall be maintainable for failure to comply with this act." The law says that the doctor must take the blood test of the patient. To be sure, the consent of the patient is required. But in making a malpractice claim the patient could, and from a previous experience in some instances would, claim that she gave the consent. That the doctor had not taken the test which the law demands could well be claimed to be malpractice. Consequently, this amendment was added to avoid malpractice suits.

L.D. 606. Lien on casualty insurance proceeds for hospitals. Not passed.

L.D. 57. Creating office of State Pathologist, earnestly supported by attorney general. Not passed.

L.D. 537. Compensation Act. Employee may select his own physician in industrial injury. Not passed.

L.D. 612. Non-profit hospital corporations authorized. Not passed.

L.D. 938. Boards of registration, including that of medicine, may suspend the license fees if and whenever there is enough money on hand to warrant it. Not passed.

L.D. 322. Incorporating the Associated Hospital Service of Maine (socialized hospital service). Passed.

L.D. 600. Optometrist Bill. Forbidding optometrists to practice when hired out, as to chain stores. Stormy career and in doubt up to the end of the Legislature. Passed, but probably ineffective for the purpose it seeks, because the chain stores employing the optometrist will have written contracts with them and probably can by injunction and in equity prevent the operation of the law to defeat their rights under the written contracts.

L.D. 755. To create a licensing department in the hands of one man to take over completely all the powers of the various boards of registration including medicine. Not passed.

L.D. 811. Permits blood grouping tests in bastardly cases and makes the testimony of the examining physician admissible (heretofore such evidence unacceptable in Maine courts). Passed.

L.D. 546. Commitment may be made of insane not only to state hospitals, as heretofore, but to government hospitals as well. Passed.

L.D. 1152. Lawsuits to recover for so-called "death without conscious suffering." Right to recover "the reasonable expense of medical, surgical and hospital care and treatment" added. Passed. Heretofore in so-called "instant death" cases, that is, those in which the deceased never recovered consciousness after the injury, such incidental expense could not be recovered.

CORRESPONDENCE

PARKING FOR DOCTORS IN A RESTRICTED AREA

To the Editor: Having been called into court for visiting a patient east of Dartmouth Street before 10:00 a. m., I wrote as President of the Society to Superintendent of Police, Edward W. Fallon, asking if some provision could be made so that doctors visiting their patients in this area, where they are trying to stop early parking, could be worked out. I thought possibly you might like to make some comment in the *Journal.*

After giving the matter consideration and consulting Deputy Superintendent John T. O'Dea, of the Traffic Division, he wrote me the following:

> It is not the aim of the Police Department to interfere in any way with a doctor making a legitimate call to answer any emergency where he is to wait upon the sick, the infirm or the injured and if any such doc-

tor will get in touch with the nearest policeman in any such cases, the officer will be only too pleased to assist the members of the Massachusetts Medical Society in every way possible.

CHANNING FROTHINGHAM, M.D.,
President, Massachusetts Medical Society.

REPORTS OF MEETINGS

HARVARD MEDICAL SOCIETY

At a meeting of the Harvard Medical Society at the Peter Bent Brigham Hospital on Tuesday, February 14, Dr. Elliott C. Cutler presided. Four cases from the medical wards were presented.

The first case, presented by Dr. Albert C. England, Jr., was a fifty-six-year-old carpenter who came in with a chief complaint of pain in the left chest of four hours' duration. When first seen in 1936 for excision of a lipoma of his left thigh, the patient gave a history of some dyspnea and swelling of the ankles. At that time his heart was moderately enlarged and there was a soft systolic murmur over the pulmonic area. Afterward the patient had had attacks of pain in his chest on exertion or emotion, a gnawing constricting substernal pain with radiation. Nitroglycerin gave moderate relief at first. The present entry four weeks previously was preceded by a sudden attack of more severe pain than usual. Physical examination showed nothing new. There were moderate arteriosclerosis, some pulmonary emphysema and slight clinical edema. The blood pressure was 220 systolic, 110 diastolic; an electrocardiogram showed abnormal T waves in all leads. In the hospital he was comfortable in bed with only slight pain.

Dr. Robert Monroe in discussing this case mentioned the fact that nitroglycerin was losing its effectiveness. The patient had been much worried, and therefore, sedation had been necessary. The diagnosis was angina pectoris.

Dr. Daniel Balad presented the second case, a fifty-five-year-old woman, who entered the second time with the same complaint she had had in October, 1937: mild palpitation, for six years, and dyspnea, for two years. At the time of the first admission, she had had a red-cell count of 1,600,000, a hemoglobin of 15 per cent, a hematocrit of 14, and a red-cell volume of 6.2 by 10^{-11} cc. Following liver and iron therapy her red-cell count went up to 4,000,000 with 75 per cent hemoglobin. A story of black stools was unconfirmed; a gastrointestinal x-ray series was negative. The patient was discharged on iron therapy. At the present admission she had a red-cell count of 2,600,000 with 26 per cent hemoglobin. She had a 3+ guaiac test on her stools. A hidden malignancy was suspected, but repeat gastrointestinal series and proctoscopy showed no abnormalities. On treatment with iron and ammonium citrate the patient's hemoglobin had gone up.

Because of the microcytosis, Dr. Marshall Fulton made a diagnosis of idiopathic hypochromic anemia. He doubted that the gastrointestinal bleeding was the cause. He said that in younger patients the picture would be consistent with chlorosis. Dr. Monroe mentioned the relation of chronic blood loss to the premenopausal, postpregnancy period of life, and added that such patients need iron continuously for some reason.

The third case was presented by Dr. C. F. Goeringer. A sixteen-year-old girl, born in Turkey, had come in the day before with the history of a swelling in her neck of two months' duration, fatigue, dyspnea on exertion, flushing easily, nervousness and excitability, and a loss of 10 pounds during the past six months. The family history revealed one case of goiter. Physical examination showed a normal temperature and blood pressure and negative heart and lungs. There was a suggestion of lid lag and tremor of the hands and tongue. There was a symmetrical, smooth, non-tender, moderately enlarged thyroid gland, and a suggestion of a bruit. The basal metabolic rate was +25 per cent. Starting two weeks previously the patient had had Lugol's solution twice a day until a few days before entry, with some betterment in symptomatology.

Dr. Cutler commented on the patient's pulse rate of 120, the moderate dermatographia and moist, warm hands, and said that he was more in favor of a diagnosis of effort syndrome than one of true Graves's disease.

Dr. Goeringer also presented the fourth case, a fifty-five-year-old woman who was admitted for treatment of a carbuncle of the neck, but whose important though not troublesome symptoms were a brassy unproductive cough of ten years' duration, difficulty in swallowing and occasional substernal pain of three years' duration, and indefinite dyspnea on exertion without signs of decompensation. Two years previously she had begun treatment at the luetic clinic on the basis of a positive blood test and an x-ray examination which had revealed an aneurysm of the ascending aorta. Physical examination showed her pupils to be regular and equal, the trachea in the midline, a tracheal tug and pulsations in the second right interspace. There was no shock or thrill. Retromanubrial dullness was increased to 12 cm. There were some signs of compression of the lung under the right clavicle. The heart was slightly enlarged to the left, and there was a systolic murmur heard along the left sternal border and in the left axilla.

Dr. Cutler commented on her lack of complaint. Treatment had been instituted for the sake of the occasional substernal pain. The diagnosis was aneurysm.

The remainder of the evening's program consisted of a talk by Dr. Reginald Fitz, the title of his dissertation being "Forsan et Haec Olim Meminisse Juvabit?" which he ultimately translated as "Every so often, for all of us, it is nice to remember things in the past."

By the narration of a dream, Dr. Fitz skillfully transferred himself and the audience back to February 14, 1898, in Baltimore at a clinic presided over by Dr. William Osler. The first case was presented by a medical student, Mr. Fulton, now Dr. Frank Fulton. The patient complained of precordial pain. Dr. Osler examined the patient himself and noted a sixty-six-year-old man resting comfortably in bed, without dyspnea. He had a slow steady pulse, and beading of the peripheral arteries. The heart was normal except for a slightly accentuated aortic second sound. Dr. Osler then commented on the rareness of the syndrome of angina pectoris in the hospital wards of the time, and went into its history. Heberden in 1768 wrote the first account of angina pectoris, and his work still stands out, even at the present day. Matthew Arnold described his own case — a most valuable record by an intelligent man. He wrote of the pain on uphill walking or exercise. His pain became much worse when he made a visit to America, being without friends and under a strain. During a picnic in the Berkshires, his boat capsized, and the sudden attack of pain almost killed him. When Arnold returned to England and his friends, the pain almost disappeared, even to the point of allowing him to play tennis. Finally one sudden severe attack was followed three days later by his death. Allan Burn, in 1809, propounded the theory that angina pectoris was probably due to coronary disease, and he called it intermittent claudication.

The second case was that of a nineteen-year-old girl who had become quite familiar to the clinic by repeated

visits. She had come in as white as a sheet, with a red-cell count of 2,000,000. She had chlorosis, a common disease of young working girls living under conditions of hard work, poor air, poor food and little exercise. Sir Andrew Clark was interested in this condition. During his time, methods of treatment were many and various. Given rest, food, fresh air and hygiene, all would get well. One favorite prescription was for tincture of cardamon, which contained the three essentials of good medicine — color, taste and harmlessness. Mr. Pratt, now the revered Dr. Joseph Pratt, presented some clinical charts on the patient. He showed how the red-cell count had improved with hygienic measures but added that the hemoglobin had not improved until she was given iron in the form of Blaud's pills. Dr. Osler's comment was that iron is a specific for chlorosis, no matter in what form it be given, so long as it is in large doses. Blaud was a local physician, in a town in France, who made a careful series of observations on his patients with chlorosis and then presented his results to the Academy, thus gaining lasting fame.

The third case presented to Dr. Osler was that of a young man of twenty-five with an exophthalmic goiter. He had "pop-eyes," perspired easily, and was restless. He had a firm smooth symmetrically enlarged thyroid. He had all the other signs of hyperactive thyroid except a rapid pulse. Dr. Osler considered the disease to be chronic, and occasionally acute, and said that some acute fulminations led to delirium and severe consequences. Basedow and Mobius and also Joffroy had written about it and noted certain signs that bore their names. Gräfe's sign pertains to lag of the upper lid: Stellwag described widening of the palpebral fissure. These men were all intensely interested in the causes of these phenomena rather than in the disease as a whole. They regarded it as the direct opposite of myxedema. Greenfield described the histopathology of exophthalmic goiter. The only treatment at that time consisted of well-meant measures such as an ice-bag to the heart, and perhaps belladonna by mouth. Jones, in 1874, attempted to subdue the hyperactive thyroid by surgery. Dr. Osler mentioned surgery as a recent innovation and very risky; William and Charles Mayo had recently reported 12 cases of which 8 had done well and 4 died. In the year 1863 Trousseau made his famous mistake; one of his patients required digitalis, since she had the heart condition associated with hyperthyroidism, but Trousseau, by mistake, prescribed tincture of iodine, ten drops a day, and found to his amazement that the drug led to clinical improvement. With his eyes open, Trousseau tested again, alternating digitalis and iodine and proved his point. Dr. Osler spoke of this as probably indicating a better prognosis for such cases in the future.

The last patient was an obviously sick young Negro. The patient had barely managed to walk into the outpatient department, and his history had been taken by young Mr. Henry Christian, who presented him to Dr. Osler. The thirty-six-year-old patient had given a history of a primary chancre ten years previously, but he had been well until two months before entry when he began having dyspnea, an upper respiratory infection and a "misery" in his chest. The last few nights he had had to sleep in a chair. Dr. Osler then demonstrated by physical examination the visible pulsation in the sternal region, with the trachea displaced to the left, carotid pulsations and cyanosis of the tongue, nailbeds and lips. The patient's breathing was notable in that expiration was longer, louder, and more jerky than inspiration, respiration being mostly abdominal and stridulous. There was a diffuse area of sternal pulsation on the right, and a displaced thyroid gland with pulsation above the right clavicle. The heart itself was normal. Examination of the lungs showed loud tracheal rales scattered throughout the chest. The patient had a hoarse voice, brassy cough and great dyspnea. The diagnosis was obviously aneurysm, probably of the innominate artery. The surgical treatment was ligation of the innominate artery, or perhaps osteotomy of the clavicle and manubrium to relieve tracheal pressure.

At this point Dr. Fitz awoke from his dream, but he had to follow up these patients. The first patient in three months had a sudden severe attack, called his family and died quietly a few days later. The last case, the patient with aneurysm, was later demonstrated by Dr. Osler at postmortem, and the diagnosis of aneurysm of the innominate artery was confirmed. Dr. Osler bewailed their lack of courage in not having operated and ligated the vessel.

Dr. Fitz explained, in answer to questions, that he had secured his data for 1898 from Dr. Joseph Pratt's beautiful notes as a medical student. Mr. Pratt had taken down Dr. Osler's lectures almost verbatim.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The New England Society of Physical Medicine met at the Ring Sanatorium and Hospital on March 15. Following a dinner served to members and guests the program was presented at Hambury Hall. Dr. Abraham Myerson, director of research, Boston State Hospital, addressed the meeting on "Combined Physiotherapeutics and Motivation in the Treatment of Chronic Schizophrenia."

Dr. Myerson said that the general principles underlying the treatment of the chronic schizophrenic by what is called the "total push" method are: (1) That mind and body are one and that mental functions can be profoundly influenced by bodily states, and vice versa; and that the division of the individual into mind and body is only a convenience and not a scientific reality. The skin of the body, naturally a place of meeting of the organism with the stimuli which pour in on it, and the muscles, which express the activity of the organism and in particular portray and discharge emotional states, have especial importance in all physiotherapeutic, psychotherapeutic relations. (2) That men live in an atmosphere of praise, blame, reward and punishment, which are the most powerful social motives for conduct and for the inhibition of conduct that exist, aside from the natural hereditary constitutional drives. (3) That use and disuse of function plays an important role in the building up of personality and character, and where functions are non-used, this creates not only atrophy but a lop-sided development of personality and character.

The chronic schizophrenic is by virtue of his disease alone a person in retreat, and this retreat is associated with delusions, especially of reference, persecution and inferiority, with corresponding disorder of physical functioning. In the hospital to which he is sent, unless a determined effort is made regardless of his own co-operation, this retreat is enhanced, since he lives in what is designated as a physiological and motivation vacuum, by which his retreat is furthered and deterioration develops. It is the theory of this "total push" method that the deterioration is an artificial product; that schizophrenia is not so profound a disorder as it seems; and that by using all available physiological and psychological measures in an organized, consecutive, day-by-day, and hour-by-hour method, with liberal administration of praise, blame, reward and, in so far as it is humanely possible, punishment,

this retreat may be halted and the patient advanced to a better mental status.

The "total push" method as used at the McLean Hospital, with the co-operation of Dr. Tillotson and his staff, has been carried out for several months on chronic and what appeared to be hopelessly deteriorated schizophrenics. The results have been surprising in the amount of improvement which has been gained physically, socially and, in a narrower sense, mentally. No cure is claimed for this procedure, and in fact, no cure is anticipated. The method, however, shows that the deterioration is not a necessary part of the schizophrenia, and we are gaining insight into the nature of the disease process.

The paper was discussed by Drs. Kenneth B. Tillotson, Curtis T. Prout, John W. Thompson and Roy D. Halloran.

NOTICES

REMOVALS

GUSTAVE B. FRED, M.D., announces the removal of his office to 520 Beacon Street, Boston.

HOLLIS L. ALBRIGHT, M.D., announces the removal of his office to 412 Beacon Street, Boston. Telephone KENmore 3750.

A WARNING

It has been reported to the *Journal* from a reliable source that a man claiming to be a medical student has entered a hospital and doctors' locker room without permission and stolen a valuable watch. This same man disappeared with money from a person who had befriended him. He goes under the name of Terry Roth or H. Barker, is 23 years old, 6 feet 1 inch, 185 pounds, has light hair, is of Jewish descent, and is hard of hearing in one ear.

Any information concerning this man would be appreciated by the chief inspector, Department of Police, Lynn, Massachusetts.

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning, 10:00 to 12:30, there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. Neoplasms of various sorts are seen and discussed, and when there is an indication, are treated with radium of high-voltage x-ray. Physicians are invited to visit this clinic. They may bring patients for aid in diagnosis or may refer patients to the clinic following which a report will be returned to the referring physician. A limited number of beds are available for diagnostic study and for treatment.

SYMPOSIUM ON CARCINOMA OF THE TONGUE

A symposium on carcinoma of the tongue has been arranged by the staffs of the Massachusetts General, Collis P. Huntington Memorial, Pondville and Palmer Memorial hospitals. A review of cases seen at each of these hospitals will be presented by Drs. Roy E. Mabrey, Ira T. Nathanson, Thomas J. Anglem and Clifford C. Franseen. Discussion will be opened by Dr. Channing C. Simmons.

The meeting will be held on Tuesday, June 13, on the roof of the Palmer Memorial Hospital, at 8:00 p. m. Refreshments will be served.

All members of the medical profession are cordially invited to attend.

LELAND S. MCKITTRICK, M.D., *Chairman.*

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION

The ninth annual convention of the Biological Photographic Association will be held September 14 to 16 at the Mellon Institute for Industrial Research, Pittsburgh, Pennsylvania. The program will be of interest to scientific photographers, scientists who use photography as an aid in their work, teachers in the biological fields, technical experts and serious amateurs. It will include discussions of moving picture and still photography, photomicrography, color and monochrome films, processing, and so forth, all in the field of scientific illustrating.

This association is prepared to make photographs for physicians and others on a nonprofit basis. Further information about the association and the convention may be obtained by writing the Secretary of the Biological Photographic Association, University Office, Magee Hospital, Pittsburgh, Pennsylvania.

INSTITUTE FOR THE CONSIDERATION OF THE BLOOD AND BLOOD-FORMING ORGANS

The University of Wisconsin Medical School is to conduct an Institute for the Consideration of the Blood and Blood-Forming Organs, September 4 to 6. Formal papers are to be presented by a group of internationally known speakers.

Physicians and others who are interested are cordially invited to attend. A detailed program may be obtained by addressing Dr. Ovid O. Meyer, Chairman of Program Committee, University of Wisconsin Medical School, Madison, Wisconsin.

MEDICAL LIBRARY ASSOCIATION

The forty-first annual meeting of the Medical Library Association will be held from June 27 to June 29, at the Academy of Medicine of Northern New Jersey, 91 Lincoln Park, Newark, New Jersey. The program will include addresses, discussions, and demonstrations on library procedure, medical history and literature.

JANET DOE, *Secretary.*

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JUNE 5

TUESDAY, JUNE 6

*10 a. m. - 12:30 p. m. Tumor Clinic. Boston Dispensary.

WEDNESDAY, JUNE 7

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

FRIDAY, JUNE 9

*10 a. m. - 12:30 p. m. Tumor Clinic. Boston Dispensary.

SATURDAY, JUNE 10

*10 a. m. - 12 m. Staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

JUNE 1 and 2 — Fourth Annual Convention of the National Gastroenterological Association. Page 857, issue of May 18.

JUNE 5, 6, 7, and 8 — American Association of Industrial Physicians and Surgeons. Page 581, issue of March 30.

JUNE 6 — Harvard Medical Alumni Association. Page 851, issue of May 18.

JUNE 6 — Tufts College Medical School Alumni. Page 851, issue of May 18.

JUNE 6 — Boston University School of Medicine Alumni Association. Page 851, issue of May 18.

JUNE 6, 7, and 8 — Massachusetts Medical Society. Worcester.

JUNE 7 — Massachusetts Medico-Legal Society. Page 851, issue of May 18.

JUNE 12-17 — Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Page 815, issue of May 11.

JUNE 13 — Symposium on Carcinoma of the Tongue. Page 941.

JUNE 26-29 — National Tuberculosis Association. Page 897, issue of May 25.

JUNE 27-29 — Medical Library Association. Page 941.

JUNE 29 — Pentucket Association of Physicians, 8:30 p. m., Hotel Whittier, 5 Washington Street, Haverhill.

AUGUST 30 - SEPTEMBER 2 — Seminar in Physical Therapy. Page 857, issue of May 18.

SEPTEMBER — Boston Psychoanalytic Institute. Page 450, issue of September 22.

SEPTEMBER 4-6 — Institute for the Consideration of the Blood and Blood-Forming Organs. Page 941.

SEPTEMBER 5-8 — American Congress of Physical Therapy. Page 857, issue of May 18.

SEPTEMBER 11-15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

SEPTEMBER 14-16 — Biological Photographic Association. Page 941.

SEPTEMBER 15-28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

OCTOBER 23 - NOVEMBER 3 — New York Academy of Medicine. Page 581, issue of March 30.

FALL, 1939 — Temperature Symposium. Page 218, issue of February 2.

MAY 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

DISTRICT MEDICAL SOCIETY

SUFFOLK SOUTH

JUNE 14 — Page 897, issue of May 25.

BOOK REVIEWS

Emotions and Bodily Changes: A survey of literature on psychosomatic interrelationships, 1910–1933. H. Flanders Dunbar. Second edition. 601 pp. New York: Columbia University Press, 1938. $5.00.

The first edition of this book appeared in 1935. This edition has not materially changed the character of the book, but there is some additional material and particularly a long introduction by the author in which she advocates the development of centers for psychosomatic study, staffed by experimental physiologists and clinicians. The book is made up of a critical bibliography, extensive in character, and apparently covering practically all the literature in its 2300 references. There are critical digests of this literature, most of them comparatively short. These have been integrated into chapters covering subjects such as acute and chronic illness, metabolism, diseases of the various systems of the body, and therapeutic considerations. In general, this is a reference book of value to scholars working in this field. It is not a book that will be of much value to the general practitioner. With the knowledge that the author possesses, however, a series of essays on her chapter headings, based on the bibliography, would be of great value to the medical profession. As it is now, the material is so diffusely presented that no conclusions can be drawn in regard to the actual importance of the research that is being reported.

Medical Information for Social Workers. Edited by William M. Champion. 529 pp. Baltimore: William Wood & Co., 1938. $4.00.

This book consists of a series of chapters written by nine physicians who have given courses of instruction at the School of Applied Social Diseases at Western Reserve University. It is designed to interest and instruct those who are engaged in the study of social work.

It is evidently the belief of these lecturers that all people engaged in this occupation should have a broad knowledge of medicine and disease in order to supplement the work of physicians in dealing with those patients who are found to have complications of a personal or environmental nature which may prevent a return to useful and enjoyable life.

Most of the important diseases are considered, but without any attempt to induce these social workers to take over the work of physicians, but rather to teach people the importance of relying on well-qualified practitioners. Emphasis is given to the useful field open to these workers in dealing with the problems of community life and public health.

The book is well written and conveys a great deal of useful information which will interest young doctors. Indeed the busy practitioner could, in many cases, profit by perusal of it. Many of the chapters convey information which the laity may also read with profit — especially that telling how to select a physician. The reviewer found nothing to criticize in this book and felt repaid for the time devoted to it.

Petite Chirurgie et Technique Médicale Courante. G. Roux. 591 pp. Paris: Masson et Cie, 1938. 90 Fr. fr.

This book is intended as a text for senior students and as a practical reference volume for the general practitioner. It fulfills its purpose admirably, covering the fields of minor surgery, gynecology, urology and otolaryngology, as well as those procedures which in English-speaking countries generally fall within the domain of "medicine." Typical Gallic orderliness and precision are reflected in the careful discussions of indications, contraindications and technic which accompany the presentation of each diagnostic or therapeutic procedure. No drug or medicine is mentioned without complete directions for its preparation, a practice which could well be adopted more often by American authors. There is a profusion of unusually fine and pertinent line drawings.

The book should enjoy a wide popularity in France and could be read with profit by the English-speaking student, intern or practitioner.

Diagnostic Roentgenology. Renewal pages 1938. 292 pp. New York: Thomas Nelson & Sons, 1938.

Short additional contributions to original articles appearing in the first issue of *Diagnostic Roentgenology* have been made as follows:

Diseases of Skull and Intracranial Contents. Dr. Cornelius G. Dyke.
Paranasal Sinuses and Mastoids. Dr. G. W. Grier.
Radiology of the Chest. Dr. Coleman B. Rabin.
Cardiovascular System. Dr. Hugo Roesler.
Digestive Tract. Dr. Ross Golden.
Diseases of the Bones. Drs. Paul C. Hodges, D. B. Phemister and Alexander Brunschwig.
Diseases of the Urinary Tract. Drs. Leopold Jaches and Marcy L. Sussman.
Uterotubography. Drs. Samuel A. Robins and Albert A. Shapira.
Obstetrics. Drs. Howard C. Moloy and Paul C. Swenson.

New chapters have been added as follows:

Dental Roentgenology. Dr. Leroy M. Ennis.
Soft Tissues of the Air and Food Passages of the Neck. Dr. Barton R. Young.
The Abdomen. Dr. Ross Golden.

The entire subject matter is well handled, the book is profusely illustrated, and the contributions are up to date. This text should prove to be a valuable reference book not only for the physician specializing in x-ray but also for the general practitioner of medicine.